ABSTRACT

Background:

After endotracheal intubation verifying the location of endotracheal tube is of utmost importance. Many methods have been applied but none is perfect. The standard practice is to use auscultation of chest with capnography. Ultrasound machines are now gaining popularity and their access extends from operation theatres, emergency rooms and even many primary health centres. Both capnography and ultrasonography are proven to be safe. This study aims to see if ultrasonography can also be made a routine method of endotracheal tube position confirmation inside operating theatres along with capnography.

Methods:

This was a prospective, observational study conducted at the Tribhuvan University Teaching Hospital (TUTH) and Manmohan Cardiothoracic Vascular and Transplant Center (MCVTC) operating rooms from January 2017 to July 2017. Ethical approval from the Institutional Review Board (IRB) of Institute of Medicine (IOM) and the Department of Anaesthesiology, Maharajgunj Medical College (MMC) was taken. Written informed consent was taken.

ASA I and II patients over 16 years of age were included in this study. Patients with difficult airway and anticipated difficult intubation, respiratory diseases, poor functional status, emergency case, and patients at risk of aspiration were excluded.

The diagnostic characteristics of real-time, suprasternal, transtracheal ultrasonography and capnography were tested by calculating their respective sensitivities, specificities, positive predictive values (PPV), negative predictive values (NPV), accuracies and likelihood ratios. Comparison of time taken for confirmation of endotracheal tube

position from the beginning of laryngoscopy, by ultrasonography versus capnography was done using t-statistics.

The degree of agreement of result between ultrasonography and capnography was tested with kappa statistics.

Results:

Out of the 95 patients studied, 11 had oesophageal intubation (Incidence of 11.57%). The overall accuracy of both ultrasonography and capnography was 96.84%. The sensitivity, specificity, PPV, NPV with their corresponding 95% confidence intervals (CI) for ultrasonography were 97.62% (91.66% - 99.71%), 90.91% (58.72% - 99.77%), 98.80% (92.67% - 99.81%), 83.33% (55.66% - 95.22%) respectively; and that for capnography were 96.43% (89.92% - 99.26%), 100% (71.51% - 100%), 100% (100% - 100%) and 78.57% (54.69% - 91.76%) respectively.

The likelihood ratio of a positive and a negative result for ultrasonography were 10.74 and 0.03 respectively, and that for capnography were infinity and 0.04 respectively.

The kappa value was 0.749 (95% CI: 0.567 – 0.931) which meant a good degree of agreement of result between these two methods.

The average time taken for confirmation of endotracheal tube by ultrasonography and capnography were 26.79 ± 7.64 seconds and 43.03 ± 8.71 seconds (mean ± standard deviation) respectively. The median time for confirmation was 26 seconds with interquartile range [15 - 37] seconds for ultrasonography and 42 seconds with interquartile range [29 - 55] seconds for capnography. Ultrasonography was found to be faster than capnography by 16.36 ± 3.23 seconds (mean ± standard deviation) and the difference in time was significant (p = 0.011).

Conclusion:

Ultrasonography and waveform capnography are both reliable and accurate methods of confirming endotracheal tube position. The use of ultrasound with capnography will help reduce time and increase precision of confirming endotracheal tube position. Ultrasound can confirm endotracheal tube position before manual bag ventilations, and thus may prevent aspiration of gastric contents into patient's lungs.

Keywords: Endotracheal intubation; ultrasonography; capnography.

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LIST OF ABBREVIATIONS

%	Percentage
>	Greater than
<	Lesser than
±	Plus– Minus
α	Alpha
ACLS	Advanced Cardiac Life Support
AHA	American Heart Association
ASA	American Society of Anesthesiologists
β	Beta
BMI	Body Mass Index
BPM	Beats Per Minute
CI	Confidence Interval
CL	Cormack Lange
CO_2	Carbon Dioxide
COPD	Chronic Obstructive Pulmonary Disease
CPR	Cardiopulmonary Resuscitation
DLT	Double-Lumen Tube
ECG	Electrocardiogram
Eg	Example
ET	Endotracheal
$ETCO_2$	End Tidal CO_2
NIBP	Non-Invasive Blood Pressure
IRB	Institutional Review Board

IOM	Institute of Medicine
IQR	Interquartile Range
κ	Kappa value
Kg	kilogram
LMA	Laryngeal Mask Airway
LR^+	Likelihood ratio of a positive test
LR^-	Likelihood ratio of a negative test
MCVTC	Manmohan Cardiothoracic Vascular and Transplant Center
MMC	Maharajgunj Medical Campus
mg	milligram
mm	millimeter
NPV	Negative Predictive Value
OT	Operation Theater
PAC	Preanaesthetic Checkup
PEEP	Positive End Expiratory Pressure
PPV	Positive Predictive Value
PVC	Polyvinyl Chloride
Sec	Seconds
SEM	Standard Error of Mean
SpO_2	Oxygen saturation of Hemoglobin
TRUE	Tracheal Rapid Ultrasound Examination
TU	Tribhuvan University
TUTH	Tribhuvan University Teaching Hospital
USA	United States of America
USG	Ultrasonography

INTRODUCTION

Endotracheal intubation is regarded as the gold standard for airway management in anaesthesia practice.[1] It establishes a definitive airway, provides maximal protection against aspiration of gastric contents, and allows for positive pressure ventilation. The modern, standard endotracheal tube is disposable, made for single-use; and is a cuffed, polyvinyl chloride tube designed to be inserted through the nasal or oral orifice. The tip of the tube sits distally at the midtrachea. Oesophageal and endobronchial intubation lead to significant anaesthesia related morbidity and mortality, which in most circumstances are avoidable.[1]

Endotracheal tube placement can be determined in the operating room by various methods[1-3]:

- Direct visualization of passage of endotracheal tube between vocal cords
- Bilateral chest rise during ventilation
- Visible condensation in the endotracheal tube
- Auscultation: equal breath sounds heard bilaterally over the chest wall and lack of breath sounds over the epigastrium
- Large exhaled tidal volumes
- Appropriate compliance of the reservoir bag during manual ventilation
- Capnography
- Fiberoptic bronchoscopy
- Ultrasonography
- Oesophageal detection devices, chest radiography which are less feasible

The ideal method for confirmation of endotracheal tube placement should be fast, simple, reliable and safe.[3] Visualization of passage of endotracheal tube through the vocal cords and waveform capnography showing sustained detection of exhaled carbon dioxide are the gold standard methods to confirm endotracheal tube placement.[4] Capnography is the most important objective method to confirm endotracheal tube placement[1]; and has been included into the ASA standards of monitoring.[5] None of these methods including capnography fulfill all the credentials of an ideal method.[3] No single method can be completely relied upon especially during emergency intubations.[6] Most of these methods require bag ventilations which may lead to aspiration of gastric contents in the advent of oesophageal intubation. Objective monitors and techniques may not be widely accessible or may be difficult to learn and operate. Therefore adjunctive methods have to be added to the current standard practice to increase precision, reduce time and prevent hazards of oesophageal intubation.[6]

Exhaled CO_2 measurement

Capnometry is the measurement and numeric representation of the carbon dioxide (CO_2) concentration during inspiration and expiration.[7] A capnograph, however, is a device that records and displays CO_2 concentrations as a function of time or volumes.[8] A time capnogram is a continuous concentration–time display graphically of the CO_2 concentration sampled from a mixture of gases at a patient's airway during ventilation. The time capnogram is divided into four distinct phases[7]:

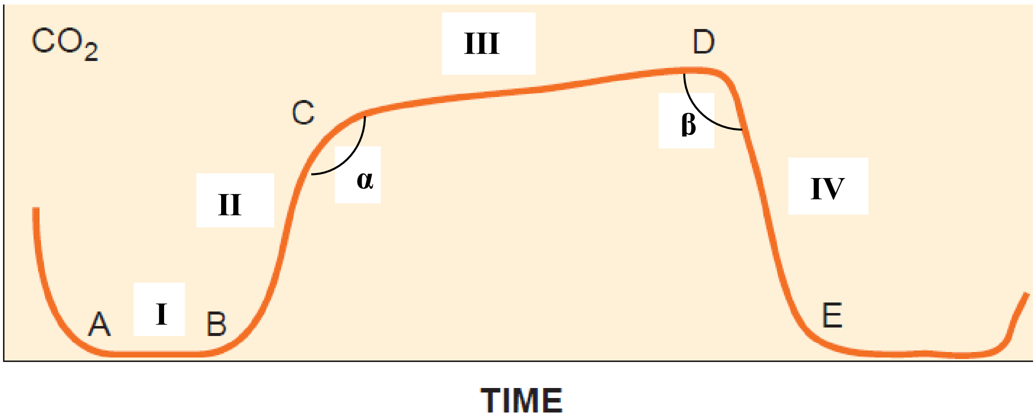


Fig.1. Normal capnogram showing a regular CO_2 waveform.[7(p705)]

The first phase [A–B], also known as phase I, represents the initial stage of expiration. Gas sampled during this phase occupies the anatomic dead space and is normally devoid of CO_2. At point B, CO_2 containing gas between the airways and alveoli presents itself at the sampling site and a sharp upstroke of the second phase [B–C] or phase II is seen in the capnogram. Phase III [C–D], represents expiratory plateau from the alveolar gas which is now sampled. There is slight up sloping of CO_2 concentration versus time during phase III due to heterogeneous distribution of ventilation-perfusion or alveolar CO_2 partial pressure throughout the lungs. The term "end-tidal" CO_2 ($ETCO_2$) generally refers to the final value of the exhaled CO_2 curve, at the very end of the expiratory phase. As the patient begins to inspire, fresh gas is entrained and there is a steep down stroke [D–E] of the phase IV, back to baseline. Unless rebreathing of CO_2 occurs, the baseline approaches zero.[7,8]

The angle between Phases II and III is called the α angle, or the takeoff or elevation angle. Normally, it is between 100 and 110 degrees. Airway obstruction, eg. during bronchospasm, and PEEP cause a larger α angle and hence an increased slope in the waveform at C-D. The angle between the end of Phase III and the descending limb of the capnogram in phase IV is called the β angle. Normally, it is approximately 90 degrees. The angle is increased with rebreathing.[2]

$ETCO_2$ is the best reflection of the alveolar CO_2 ($PACO_2$). The $ETCO_2$–$PACO_2$ gradient typically is around 5 mm Hg during routine general anaesthesia in otherwise healthy, supine patients. $ETCO_2$ value usually ranges between 35-45 mm of Hg.[7] The presence of CO_2 in exhaled breath assures the anaesthesiologist of correct placement of an endotracheal tube or laryngeal mask airway (LMA), as well as the integrity of the breathing circuit.[8]

$ETCO_2$ monitoring devices fall into 3 categories: colorimetric (changes color), capnometric (numeric; quantitative display), or capnographic (numeric display with waveform; qualitative display). Colorimetric devices require sufficient exhalation time up to 6 successive ventilations for change of color to occur. A perfusing cardiac rhythm and uncontaminated device are the prerequisites of these devices. Airway secretion affect the reliability of the colorimetry.[9] They are now rarely available commercially.

The most commonly used method of detecting CO_2 in respiratory gases is non-dispersive infrared absorptiometry. Absorption of infrared light by CO_2 is governed by the Beer–Lambert law.[8] There are two general categories of capnographs: sidestream (diverting) and mainstream (nondiverting). Sidestream analyzers have CO_2 sensors physically located away from the endotracheal tube and ventilator circuit to measure airway gases. Sidestream analyzers have a transport delay time corresponding to the rate at which gas is sampled from the anaesthesia ventilator circuit. The time delay is also affected by the rate of washout of previously sampled gas from the analyzing chamber. In mainstream analyzers, the sample sensor cell is placed directly into the patient's breathing circuit. The inspiratory or expiratory gases pass directly through the infrared light path and thus they have no delay time.[8]

The presence of exhaled CO_2 for six successive breaths indicates that the endotracheal tube is not in the oesophagus. Most capnographs provide a quantitative $ETCO_2$ value (capnometry) as well. However it is the capnography reading of regular waves and not sole quantitative $ETCO_2$ value that is the gold standard for endotracheal tube confirmation.[10] CO_2 may be falsely read by capnometers initially because of presence of CO_2 due to gastric insufflation during bag and mask ventilation, or due to ingestion of carbonated drinks by the subject. The $ETCO_2$ value slowly decreases to undetectable during oesophageal intubation in such cases.[3,9,10] In the event of oesophageal intubation, the six breaths allow the CO_2 in the stomach to disperse.[11] The capnogram will have an abnormal configuration and be irregular in such cases.[2] An $ETCO_2$ value greater than or equal to 5 mm of Hg after six ventilations also suggests that the endotracheal tube is not in the oesophagus.[12]

In a study comparing auscultation, capnometry and capnography for endotracheal tube confirmation, Grmec[12] found that auscultation is unreliable compared to capnometry and capnography. While the sensitivity and specificity of capnography were both 100% in 345 emergency intubations including both cardiac arrest and non-arrest patients, the sensitivity and specificity of capnometry were 88% and 100% respectively. In their study, there were 28 false negatives in capnometry which were all cardiac arrest cases. Similar results showing better reliability of capnography over capnometry was found by Ornato et al[13], Macleod et al[14], and Bozeman et al[15].

A continuous, stable CO_2 waveform ensures the presence of alveolar ventilation but does not necessarily indicate that the endotracheal tube is properly positioned in the trachea. Endotracheal tube placed proximally to the vocal cords may still produce an otherwise satisfactory tracing until it becomes dislodged. An endobronchial intubation cannot be ruled out until breath sounds are auscultated bilaterally. Capnography is also unreliable for endotracheal tube confirmation during low pulmonary flow states, and also during bronchospasm or a kinked endotracheal tube.[4] Though the American Heart Association (AHA) has incorporated presence of capnograph waveforms and $ETCO_2$ value greater than 10 mm of Hg as sign of effective chest compressions in the Advanced Cardiac Life Support (ACLS) algorithm[16]; capnography is regarded to be unreliable during cardiopulmonary resuscitation[1,2,7] and also with adrenaline use.[6]

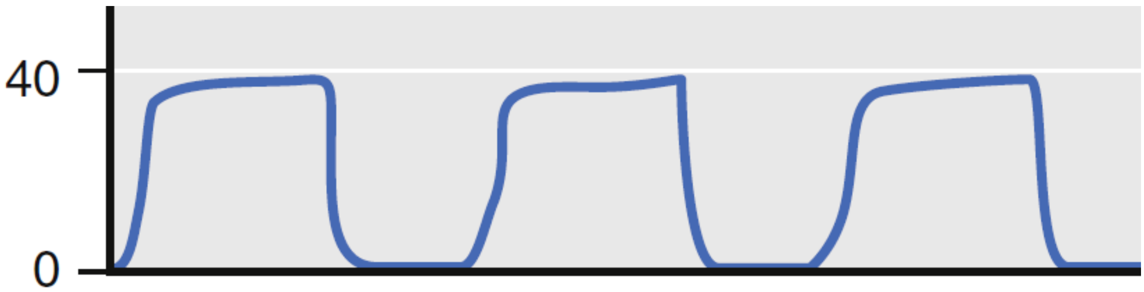


Fig. 2. Normal waveform capnogram during tracheal intubation.[8(p1554)]

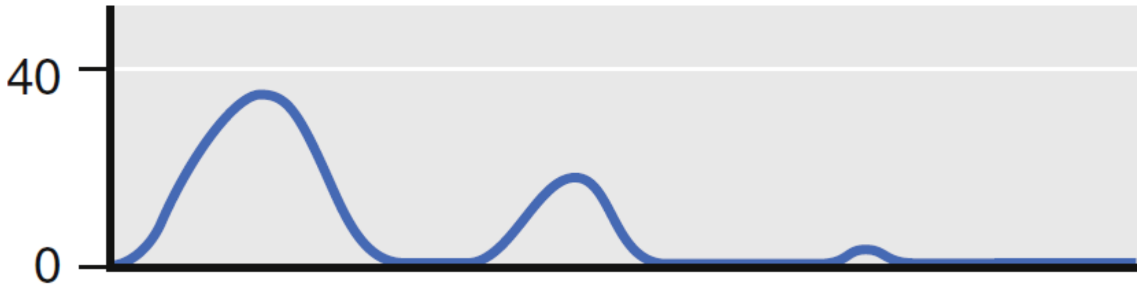


Fig. 3. Irregular waveform capnogram during oesophageal intubation.[8(p1554)]

Ultrasonography

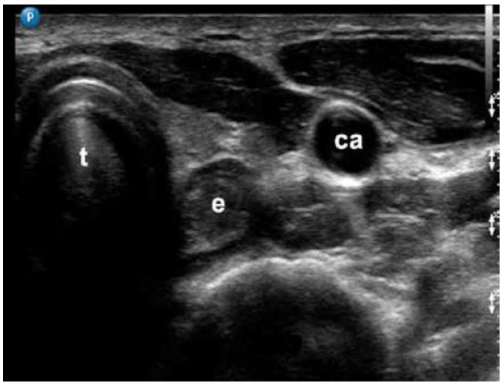
Ultrasonography is now being increasingly used in medical practice as a bedside point of care utility. It is safe, quick in learned hands, portable and widely available in different departments of a hospital or other health facilities.[17] Applications of ultrasound imaging in airway management can be as follows[17,18]:

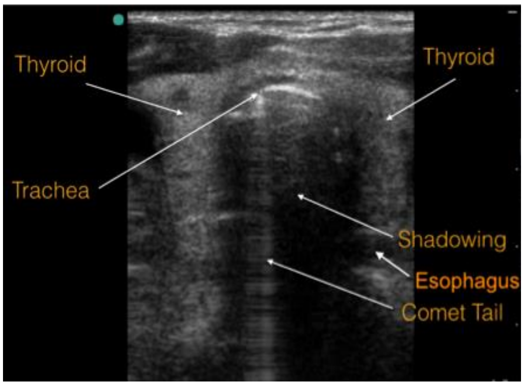
- Identification of position of endotracheal tube during intubation
- Assessment of the diameter of the subglottic upper airway and prediction of endotracheal tube size, including pediatric endotracheal tube size and double-lumen tube size
- Detection of subglottic stenosis, prediction of post-extubation stridor
- Guidance of percutaneous dilatational tracheostomy and cricothyroidotomy
- Prediction of difficult intubation through measurements of various airway parameters
- Ultrasound-guided upper airway anaesthesia to facilitate awake intubation
- Detection of laryngeal mask airway position
- Diagnosis of upper airway pathologies, e.g. soft tissue masses

For the purpose of endotracheal tube confirmation, a high frequency linear ultrasound probe (9 – 13 Megahertz) is used. The probe is placed in transverse orientation just 0.5 to 1 cm above the suprasternal notch (Fig. 4).[19]

Normally trachea appears as a hyperechoic curvilinear structure with comet-tail artifact and shadowing (reverberations from the air-mucosa interfaces). The oesophagus is usually seen more distally, posterolateral and to the left of trachea, as an oval structure with concentric layers comprising of hyperechoic wall layers and hypoechoic center (Fig. 5).[19,20]

Fig. 4. Position of linear ultrasound probe just above the suprasternal notch.





(A) **(B)**

Fig. 5. (A) Normal suprasternal airway anatomy in ultrasound.[20]
(B) Ultrasound image focused to show trachea and oesophagus. Comet tail artifact inside the curvilinear acoustic shadow of the trachea is seen.[19]
(t=trachea, e=oesophagus, ca=common carotid artery)

The operator should slide and maintain the transducer probe slightly to the patient's left and optimize the image depth to ensure that the posterior position of oesophagus is well visualized.[20]

Successful endotracheal intubation will demonstrate an increase in artifact and shadowing in the region of the trachea only. Performing a slight shaking of the ET tube will only show movement and fluttering inside of the trachea. If color Doppler is used during the movement of the tube, a color ray will be seen inside the tracheal acoustic shadow (Fig. 6).[19]

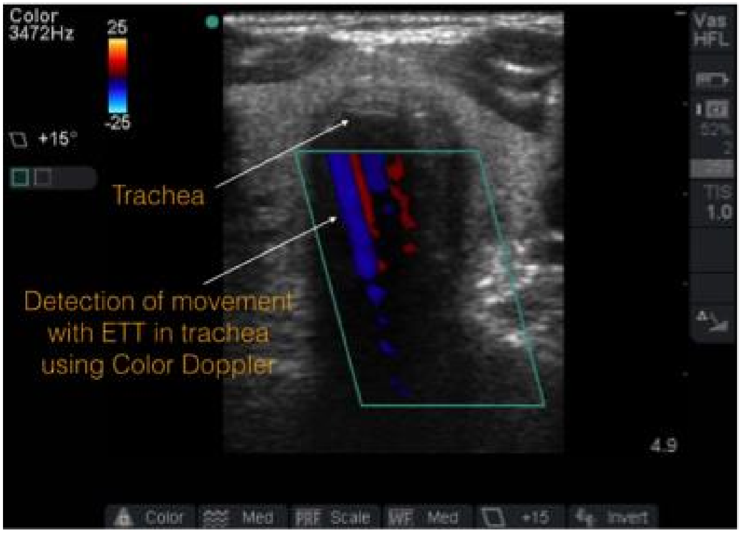


Fig. 6. Presence of endotracheal tube in trachea in Color Doppler.[19]

In oesophageal intubation, real-time ultrasound will reveal an adjacent hyperechoic curvilinear structure with shadowing being manipulated through the oesophageal lumen, and comet-tail artifact posterolateral to the trachea, (double tract sign).[19] Absence of these signs indirectly confirms tracheal placement of the tube. (Fig. 7)

If the oesophagus is located directly posterior to the trachea, an oesophageal intubation may be missed as this second hyperechoic structure will be obscured by the shadowing from the trachea.[19] To minimize this, as mentioned earlier, the probe has to be adjusted slightly to the left side of neck for proper visualization of the oesophagus including its posterior wall, prior to passing of the endotracheal tube.[20] Limitations of ultrasound also include wave scattering and acoustic artifacts generated in air-mucosa interfaces. Similarly presence of anatomical abnormalities in anterior neck and trauma or infection at the anterior neck, hamper the use of ultrasound at the suprasternal site.[18]

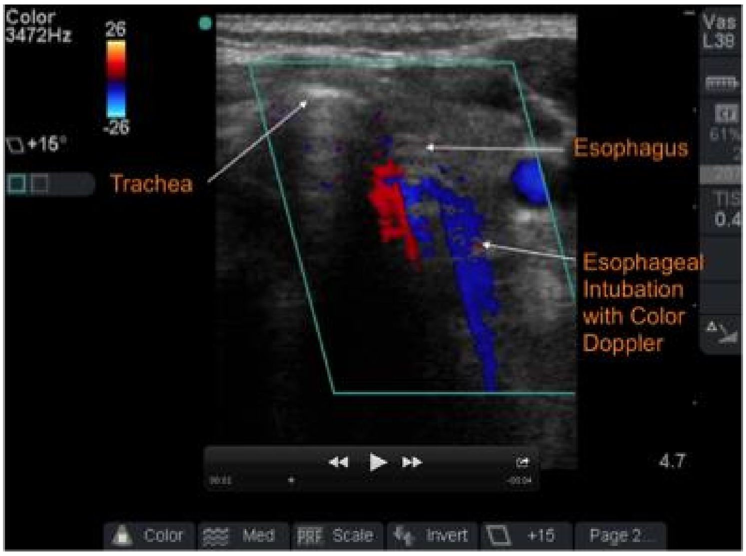


Fig. 7. Endotracheal tube in the oesophagus in ultrasound image. Presence of color Doppler ray outside of the trachea along with double tract sign.[19]

Another method described is to place the probe in transverse orientation at the level of vocal cords and see for fluttering at vocal cords or vocalis ligament in ultrasound as the endotracheal tube passes through. Tracheal ultrasound can also be done at the cricothyroid membrane level to see the placement of endotracheal tube.[18] Additional sonographic way to identify endotracheal tube placement confirmation includes visualizing bilateral lung sliding while bagging the paralyzed patient.[17]

As opposed to capnography and auscultation, ultrasonography enables clinicians to identify oesophageal intubation prior to delivering ventilatory breaths through the endotracheal tube, potentially decreasing the risk of gastric insufflation and subsequent aspiration.

Tracheal ultrasonography is not affected by low pulmonary flow or bronchospasm unlike in capnography.[1,17,20]

The current practice in anaesthesia is to use the combination of auscultation and capnography waveform observation for endotracheal tube confirmation in most centres including in IOM (Institute of Medicine), at TUTH (Tribhuvan University Teaching Hospital) and MCVTC (ManMohan Cardiothoracic Vascular and Transplant Center). But the capnography infrared sensor monitors are not widely available in Nepal. Also the matter of endotracheal tube confirmation is sensitive, it has to be done quickly prior to decreasing oxygen levels in the patient and aspiration of stomach contents into lungs has to be prevented. The practice of using capnography and auscultation requires repeated manual ventilations for endotracheal tube confirmation, and thus frequently falls short in this matter when compared to ultrasonography.[3,6,21]

Rationale

Both capnography and ultrasound are safe and have been shown to be reliable methods of endotracheal tube confirmation in previous studies which will be detailed further in literature review section. Physicians with basic knowledge about these methods can use them in operating rooms and also in emergency rooms and wards. Ultrasound machines are now gaining popularity and their access extends from operation theatres, emergency rooms and even many primary health centres in Nepal.

Conducting this study will help us to see if ultrasound when used along with capnography can reduce time taken and increase precision for endotracheal tube confirmation inside operating theatres; and further advocate use of ultrasound imaging prior to manual ventilation for endotracheal tube confirmation in full stomach or patients at risk of aspiration.

LITERATURE REVIEW

A review article published in Journal of Intensive Care Medicine, October 2009 by Rudraju and Eisen[3] discussed the effectiveness and pitfalls of the conventional and unconventional methods of endotracheal tube confirmation. None of the methods they reviewed had 100% sensitivity and 100% specificity. The best sensitivity and specificity in their opinion would be possessed by fiberoptic bronchoscopic visualization of the carina, trachea and bronchi. But this would be impractical because of availability constraint and inexperience of the operator. Secretions, blood or gastric contents would hamper fiberoptic visualization as well. The visualization of passing of endotracheal tube into the vocal cords was also stated to be unreliable. They have cited anatomical irregularities like large tongue, prominent teeth, short neck and blood and secretions as causing difficulty in visualization of vocal cords frequently.[22] They have concluded that waveform capnography would be the best practical and reliable method through numerous citations.[12,22-24] Similar conclusion was also reached by DeBoer et al[9] in their review article. In conditions where capnography could be unreliable as in cardiac arrest and bronchospasm, they have suggested few alternatives. Oesophageal suction detection devices could be useful as these do not require presence of pulmonary blood or airflow, but they have cited these devices to have low sensitivity of 80% and good specificity of 97%.[25] They have suggested ultrasonography to be good alternative method but they argued that more studies were required to establish ultrasound use during intubation.[3]

In a study done by Knapp et al[26] in 1999, they evaluated four different methods of endotracheal tube position confirmation: auscultation, capnography, oesophageal detection device which operated using suction, and transillumination method with a lighted stylet wand. They enrolled 38 participants. The subjects were first tracheally intubated and connected to a ventilator. Then a second endotracheal tube was passed into the oesophagus by laryngoscopy. Two blinded examiners, one an experienced (4 years worked in critical care) and another inexperienced (medical student) were then asked to identify the position of one of the tubes each in a subject, using one of the four methods. The method to be used to verify tube position, and the particular tube to be identified in a subject by an examiner, were randomized using allocation numbers. At the end of 152 examinations, both examiners correctly identified the tube position using capnography in all cases. Using auscultation, experienced examiner was correct in all cases, but the inexperienced examiner was correct in 68% cases only. Using the oesophageal detection device, there were two wrong results by experienced examiner and one wrong result by the inexperienced examiner. Using the transillumination method, the experienced examiner was wrong in 16% cases and the inexperienced examiner was wrong in 13% cases. Thus, capnography was found to be the most reliable method of endotracheal tube confirmation followed by oesophageal detection device. Capnography was statistically superior to auscultation and transillumination. Oesophageal detection device did not show statistical superiority to auscultation and transillumination however. They also concluded that auscultation is largely dependent on the experience of the operator.[26]

Grmec[12] also found similar results as that of Knapp et al[26] when comparing auscultation, capnometry and capnography for endotracheal tube confirmation. He tested 345 emergency intubations in a prehospital unit at Maribor, Slovenia from February 1998 to February 2001. 246 were cardiac arrest patients and 79 were non-cardiac arrest patients. In non-arrest patients, capnometry had both sensitivity and specificity of 100%; capnography also had both sensitivity and specificity 100% but auscultation had sensitivity of 94% and specificity of 83% in confirming endotracheal tube placement. Capnometry was highly specific (100%) but not sensitive (88%) for correct endotracheal intubation in patients with cardiopulmonary arrest while capnography again had both sensitivity and specificity of 100%. They concluded that capnography was the most reliable method to confirm endotracheal tube placement in emergency conditions in the prehospital setting.[12]

A meta-analysis was done by Li[24] on the use of end tidal CO_2 detection methods for endotracheal tube confirmation. 512 trials were processed from the National Institute of Health (USA) database from 1996 to 1999. Trials that included human subjects in whom emergency endotracheal intubation had been done, where the tube position was checked by a device measuring end tidal CO_2 and the result compared with another method of verification of tube position as standard, were chosen. He also excluded trials where number of tracheal and oesophageal intubations were not shown as part of the secondary objective. 10 trials were finalized and 2192 intubation were included. Tube placement for 444 out of 2192 intubations (20%) had been tested with infrared devices, and placement for 1748 out of 2192 intubations (80%) had been tested with colorimetric devices. The results showed an aggregate sensitivity of 93% (95% confidence interval (CI): 92 – 94%) and an aggregate specificity of 97% (95%

confidence interval (CI): 93 - 99%) of capnography devices for emergency endotracheal tube placement confirmation. The false-negative failure rate (tube in trachea but capnography reported oesophagus) was 7% and the false-positive rate (tube in oesophagus but capnography reported trachea) was 3%. This was translated to potential harm for one patient in every 10 emergency intubations verified with exhaled CO_2 device alone. Two trials among the ten included, reporting on 721 intubations (33% of the total), had demonstrated no difference in accuracy between the colorimetric or infrared devices end-tidal capnography for tube placement confirmation during emergency airway management. Secondary objectives were to see the rate of unanticipated oesophageal placement during emergency intubation and quantification of the portion of intubations performed in patients with cardiac arrest. The data was taken from the National Emergency Airway Registry. Of 4602 consecutive intubations, 4% of emergency intubation attempts had resulted in accidental oesophageal intubation, and 10% had occurred in non-traumatic cardiac arrest patients. He concluded that misidentification of oesophageal endotracheal tube placement in the emergency setting may occur with capnography. His recommendation was to use multiple methods of tube placement confirmation method because no single method has perfect accuracy.[24]

Chou et al[6] did a systematic review and meta-analysis to check the evidence of diagnostic value of ultrasonography for the assessment of endotracheal tube placement in adult patients. Any method of ultrasonography to confirm endotracheal tube placement was selected. Exclusion criteria included case reports, comments, reviews, guidelines and animal studies. 1334 studies were processed, 75 of these were selected. A total of 12 eligible studies were taken for final analysis which had 1656 intubation attempts. Tracheal ultrasonography was used in ten studies and lung ultrasonography was used in four studies, two studies used both tracheal and lung ultrasonography to confirm endotracheal tube placement. Seven studies used capnography or $ETCO_2$ detectors as criterion standard of tracheal intubation whereas the remaining studies used direct laryngoscopy, chest auscultation, or chest radiography. For detection of oesophageal intubation, the pooled sensitivity of ultrasonography was 0.93 (95% CI: 0.86–0.96) and the specificity was 0.97 (95% CI: 0.95–0.98). The positive and negative likelihood ratios were 26.98 (95% CI: 19.32–37.66) and 0.08 (95% CI: 0.04–0.15) respectively. A hierarchical summary receiver operating characteristic curve that plots sensitivity versus specificity was constructed and the area under the curve was calculated to be 0.97 (0.95–0.98). In tracheal ultrasonography, attending physicians demonstrated superior sensitivity (0.98, 95% CI: 0.96–0.99) when compared to resident physicians (0.92, 95% CI: 0.78–0.96). Tracheal ultrasonography performed in the emergency had a lower sensitivity (0.88, 95% CI: 0.76–0.94) in comparison to other settings. Tracheal ultrasonography performed in real-time was associated with superior sensitivity (0.94, 95% CI: 0.86–0.98) than that performed post-intubation in static manner (0.91, 95% CI: 0.70–0.98). They concluded that ultrasonography had high diagnostic value for identifying oesophageal intubation. They recommended ultrasonography be used as a valuable adjunct in endotracheal intubation confirmation, especially in situations where capnography may be unreliable.[6]

A systematic review and meta-analysis was also done by Das et al[21] in 2015 to evaluate the diagnostic accuracy of transtracheal ultrasound in detecting endotracheal intubation. Eleven studies and 969 intubations were included in the final analysis.

Eight studies and 713 intubations had been performed in emergency situations and the others were carried out in elective situations. Transtracheal ultrasonography's pooled sensitivity and specificity with 95% confidence interval (CI) were 0.98 (95% CI: 0.97 - 0.99) and 0.98 (95% CI: 0.95 - 0.99) respectively. In emergency scenarios, transtracheal ultrasonography showed an aggregate sensitivity and specificity of 0.98 (95% CI: 0.97 - 0.99) and 0.94 (95% CI: 0.86 - 0.98) respectively. Transtracheal ultrasound was concluded to be a useful tool to confirm endotracheal intubation. They recommended that transtracheal ultrasonography could be used as a preliminary test for endotracheal intubation before final confirmation by capnography.[21]

Karacabey et al[27] did a study to evaluate accuracy and speed of ultrasonography for confirming endotracheal tube placement by tracheal ultrasound and lung sliding. They also observed the degree of agreement of ultrasonography when used for endotracheal tube confirmation along with capnography as the standard method. The study was a prospective, single-centre, observational study conducted in the emergency department of a tertiary care hospital. Patients who had emergency intubation because of respiratory failure, cardiac arrest or severe trauma were included. A total of 115 patients were included in the study. Among 115 patients, 30 were cardiac arrest patients. The overall accuracy of the ultrasonography in their study was 97.18% (95% CI: 90.19% – 99.66%), and the value of kappa was 0.869 (95% CI: 0.77 – 0.96) indicating a high degree of agreement between ultrasonography and capnography. Ultrasonography took significantly less time than capnography, mean of 5.8 seconds versus 11.7 seconds respectively.[27]

Chou et al[28] in 2010 had compared real-time suprasternal transtracheal ultrasound to waveform capnography as the standard for endotracheal tube confirmation. The position of trachea was identified by a hyperechoic air–mucosa interface with posterior reverberation artifact (comet-tail artifact). The endotracheal tube position was defined as endotracheal if single air-mucosa interface with comet-tail artifact was observed. A total of 112 emergency intubations were included in the analysis, and 17 (15.2%) had oesophageal intubations. The overall accuracy of the ultrasound was 98.2% (95% CI: 93.7–99.5%). The kappa value was 0.93 (95% CI: 0.84–1.00), indicating a high degree of agreement. The sensitivity, specificity, positive predictive value, and negative predictive value of the ultrasound were 98.9% (95% CI: 94.3–99.8%), 94.1% (95% CI: 73.0–99.0%), 98.9% (95% CI: 94.3–99.8%) and 94.1% (95% CI: 73.0–99.0%) respectively. The median operating time of the ultrasound was 9.0 sec [Interquartile Range (IQR): 6.0 - 14.0 sec].[28]

Chou and his colleagues did another study[29] from 2010-2012, using the same method of real-time suprasternal tracheal ultrasonography for assessing endotracheal tube position during cardiopulmonary resuscitation, but this time they had limited their ultrasound use time to not more than 10 seconds. They tested the diagnostic accuracy of ultrasonography in a limited time frame of 10 seconds. Among the 89 patients enrolled, 7 (7.8%) had oesophageal intubations. The sensitivity, specificity, positive predictive value, and negative predictive value of tracheal ultrasonography in this study were 100% (95% CI: 94.4–100%), 85.7% (95% CI: 42.0–99.2%), 98.8% (95% CI: 92.5–99.0%) and 100% (95% CI: 54.7–100%) respectively. Positive and negative likelihood ratios were 7.0 and 0.01 respectively. Thus they concluded that ultrasound had a good diagnostic ability to detect endotracheal intubation, and the confirmation could well be performed under 10 seconds. They had used capnography as the standard method of endotracheal tube confirmation after the results of ultrasound were obtained, and they had not seen the time taken for confirmation by capnography.[28,29]

Adi, Chaun and Rishya[30] published a study in Critical Care Ultrasound Journal in 2013. They compared bedside upper airway ultrasonography to waveform capnography for verification of endotracheal tube location after intubation. It was a prospective, observational study conducted at a single centre in Taiwan. The study included patients who were intubated in the emergency department from 28 March 2012 to 17 August 2012. They scanned the anterior area of neck of patients first in horizontal view to see two parallel hyperechoic lines in trachea for tracheal intubation or absence of this with dilatation of oesophagus in oesophageal intubation. Then they reconfirmed with ultrasound in the vertical view to see for presence or absence of two hyperechoic lines. A sample of 107 patients was finalized based on the desired precision of 95% in detecting sensitivity, specificity and number of oesphageal intubations from the data of the study done by Chou et al[28]. The incidence of oesophageal intubation was 5.6%. The overall accuracy of bedside upper airway ultrasonography was 98.1% (95% CI: 93.0% - 100.0%). The kappa value (K) was 0.85, indicating a very good agreement between the bedside upper airway ultrasonography and waveform capnography. The sensitivity, specificity, positive predictive value and negative predictive value of bedside upper airway ultrasonography were 98.0% (95% CI: 93.0% - 99.8%), 100% (95% CI: 54.1% - 100.0%), 100% (95% CI: 96.3% - 100.0%) and 75.0% (95% CI: 34.9% - 96.8%) respectively. The likelihood ratio of a positive test was infinite and the likelihood ratio of a negative test was 0.0198 (95% CI: 0.005 - 0.0781). The mean confirmation time by ultrasound was 16.4 seconds. They concluded that ultrasonography could be used as an alternative of waveform capnography in confirming endotracheal tube placement in centres without capnography.

Pfeiffer et al[31] did a prospective, observational study in 2010 comparing the time taken by bilateral lung ultrasound (observing lung sliding) with auscultation and capnography for verifying endotracheal intubation. Two separate investigators, one reading the capnograph and the other performing ultrasound, were blinded from each other while performing endotracheal intubation in a patient inside an operating theatre. Both methods were thus used at once in a patient. Both methods correctly verified endotracheal tube placement in all 25 patients. Comparing ultrasound with the combination of auscultation and capnography, median time for ultrasound was 40 seconds [Interquartile Range (IQR): 35 – 48 sec] vs. 48 seconds [IQR: 45 – 53 sec], $p<0.0001$. Mean difference was -7.1 sec in favour of ultrasound (95% CI: 9.4 - 4.8 sec). Median time for auscultation alone was 42 sec [IQR: 37 – 47 sec], $p= 0.6$, with a mean difference of -0.88 sec in favor of ultrasound (95% CI: 4.2 – 2.5 sec). Thus they concluded that verification of endotracheal tube placement with ultrasound is as fast as auscultation alone and faster than the standard method of auscultation and capnography.

Gottlieb et al[32] conducted a blinded, randomized trial in 2014 designing a 4 step technique of using ultrasound to check endotracheal tube position in two human cadaver models, one thin and the other obese. The technique in short was a transtracheal ultrasound at the transcricothyroid level with the probe tilted 30 degrees towards the left from midline in horizontal view. They would shake the endotracheal tube to see for artifact inside the trachea. If no tube was seen, the probe was moved to right of neck to see for similar artifact inside the oesophagus. Three ultrasound experts and 45 emergency medicine residents performed a total of 150 scans. Experts had a sensitivity of 100% (95% CI: 72% - 100%) and specificity of 100% (95%CI: 77% - 100%) on thin cadaver, and a sensitivity of 93% (95% CI: 66% - 100%) and specificity of 100% (95% CI: 75% - 100%) on obese cadavers. Novice residents had a sensitivity of 91% (95% CI: 69% - 98%) and specificity of 96% (95% CI: 76% - 100%) on thin, and a sensitivity of 100% (95% CI: 82% - 100%) specificity of 48% (95% CI: 27% - 69%) on obese cadavers. The overall mean time to detection was 17 seconds (95% CI: 13 seconds to 20 seconds; range: 2 - 63 seconds) for experts and 29 seconds (95% CI: 25 seconds to 33 seconds; range: 6 - 120 seconds) for residents. Their ultrasound technique was accurate and rapid for ultrasound experts. Among novices, their technique was accurate in thin, but less accurate in obese cadavers.[32]

Two recent articles about ultrasound use during intubation for endotracheal tube position confirmation have been published in 2017.

Nasreen et al[33] did a study to determine the diagnostic accuracy of Tracheal Rapid Ultrasound Exam (TRUE) for detection of endotracheal tube placement. They used transverse suprasternal ultrasound method and verified tube position later with a lateral neck x-ray. Out of the 230 patients studied; the sensitivity, specificity, PPV, NPV and diagnostic accuracy of TRUE for detection of endotracheal tube placement taking lateral x-ray neck as gold standard were 98.80%, 95.24%, 98.21%, 96.77% and 97.83% respectively.

Chintamani et al[34] did a prospective, observational study was on 100 patients requiring tracheal intubation for general anaesthesia and used both capnography and transverse, suprasternal transtracheal static ultrasound after intubation to confirm the endotracheal tube placement. Ultrasound detected all five cases of oesophageal intubation, but could not detect five patients with correct tracheal intubation. Ultrasonography had a sensitivity of 96.84% (95% confidence interval [CI]: 94.25% - 96.84%), specificity of 100% (95% CI: 50.6% – 100%), positive predictive value of 100% (95% CI: 97.3% – 100%) and negative predictive value of 62.5% (95% CI: 31.6% – 62.5%) when compared to capnography as the standard method for endotracheal tube confirmation. Kappa value was found to be 0.76, indicating a good agreement between ultrasonography and capnography for confirmation of endotracheal tube placement. Time taken for confirmation of endotracheal tube was 8.989 ± 1.043 sec by capnography versus 12.0 ± 1.318 sec by ultrasound ($p < 0.001$).

OBJECTIVES

General:

To compare ultrasonography imaging and waveform capnography for endotracheal intubation confirmation in a tertiary hospital operating room setting.

Specific:

1. To determine the time taken by real-time ultrasonography imaging in detecting endotracheal tube placement.
2. To determine the time taken by capnography waves in detecting endotracheal tube placement.
3. To calculate the sensitivity and specificity of capnography and ultrasonography in detecting endotracheal tube placement.
4. To calculate positive and negative predictive values of these two methods in detecting endotracheal tube placement.
5. To interpret the degree of agreement of result obtained with ultrasonography and capnography using kappa statistics.

HYPOTHESIS

Transtracheal ultrasonography and waveform capnography are both accurate methods of verifying endotracheal tube placement after intubation.

Real-time transtracheal ultrasound is a faster method of detecting endotracheal tube placement compared to waveform capnography.

METHODOLOGY

Study design

Research Method: Qualitative and quantitative.

Type of study: Prospective, observational.

Study Population: Patients admitted for elective surgery at Tribhuvan University Teaching Hospital (TUTH) and Manmohan Cardiothoracic Vascular and Transplant Center (MCVTC) under general anaesthesia.

Study site: Operating rooms, TUTH and MCVTC.

Duration of study: 6 months. The study was conducted at MCVTC from January 17, 2017 to April 14, 2017. It was continued at TUTH from April 15, 2017 to July 14, 2074.

Sampling Method: Non-probability sampling.

Sample size: Total 95 patients were taken for analysis.

The formula for sample size with (1 -α)% confidence level and with maximum margin error of estimate of "d" for constructing confidence interval of true value of sensitivity or specificity using normal approximation is given as follows[35]:

$$n = \frac{Z_{\frac{\alpha}{2}}^{2}\widehat{P}(1-\widehat{P})}{d^{2}}$$

Where $\widehat{P}$ is pre-determined value of sensitivity or specificity that is ascertained by previous published data or clinician experience or judgment.[35]

For $\alpha = 0.05$, $Z_{\alpha/2}$ is inserted by 1.96.[35,36]

Excerpted from the meta-analysis done by Chou et al[6] where they found the sensitivity and specificity of suprasternal transtracheal ultrasound for endotracheal tube confirmation to be 0.98 and 0.94 respectively, the specificity value for $\widehat{P}$ in the equation was taken. Hence setting margin of error "d" at 5%, we could equate to:

$n = 1.96^2 \times 0.94 \times 0.06 / 0.05^2 = 86.66$

Adjusting for 10% drop outs and defaulters, a sample size of 95 was thus taken.

Inclusion criteria:

ASA I and II patients of both sexes above 16 years of age undergoing general anaesthesia with endotracheal tube placement.

Exclusion criteria:

- Patient refusal
- ASA physical status III and above
- History of prior difficult bag and mask ventilation or difficult intubation
- History of prior oro-nasal or neck injuries, burns or scars
- Active oral, pharyngeal or tracheal infection or inflammatory changes
- Anticipated difficult airway or difficult intubation during preanaesthetic examination, with Mallampati grades II and above
- Lung parenchymal and pleural diseases. Examples: asthma, COPD, bronchiectasis, reactive lung diseases, pneumonia, tuberculosis, pleural effusion, pneumothorax, lung or pleural malignancy etc.
- Emergency surgery

- Patients with known oesophageal pathology. Examples: oesophageal carcinoma, stricture, tracheoesophageal fistula etc.
- Full stomach or patients at risk of aspiration, e.g. pregnancy
- Patients with a nasogastric tube in situ
- NYHA grade 2 and above

Materials and Methods

The study was conducted inside the operating room no. 2 and 3 of MCVTC where capnography was available. These had Drager Fabius Plus, 2013 anaesthesia machine (ref: 8606800-48); Drager Infinity Delta, 2012 monitor (ref: MS18597); and Drager Scio Four, 2012 sidestream capnograph with capnometer (ref: 6871804), which had flow rate of 250ml/min and system response time of < 4 seconds. The ultrasound machine used in MCVTC was Sonosite M Turbo, 2013 (ref: P08189-83) made by Fujifilm Sonosite Inc. USA.

The study was also conducted in operating rooms 1, 2 and 7 of TUTH. These had Drager Fabius Plus, 2013 anaesthesia machine (ref: 8606800-51). The monitor used in OT 1 and 2 was Nihon Kohden BSM-2301K, 2008 which had a mainstream capnometer with identification number TG-101T (2013). The monitor used in OT 7 was Spacelabs Ultraview-SL 2700, 2013 which had a sidestream capnograph with identification number MDL-90499. The capnography module had sample line flow rate of 50ml/min ± 10ml/min and system response time of < 3 seconds. The ultrasound machine used was Sonosite M Turbo, 2015 (ref: P17000-15).

Ethical approval from the Institutional Review Board (IRB) of Institute of Medicine (IOM) and the Department of Anaesthesiology, Maharajgunj Medical College (MMC) was obtained on January 16, 2017.

Eligible patients were evaluated one day prior to surgery. Written informed consent was taken (Appendix B). Patients were kept nil per oral at least 6 hours prior to surgery. Premedication with Tablet Diazepam 0.25mg/kg body weight per oral was given on the evening before and the morning of surgery.

Intravenous line was opened with a 18 Gauge Cannula in the non-dominant hand in the operation theatre (OT) recovery area. Patient was given 0.025 mg/kg of Injection Midazolam prior to shifting to the operating room. Baseline vital parameters: NIBP, heart rate and SPO_2 were recorded at the OT recovery by the researcher.

The personnel involved in this study were:

1. Ultrasound machine operator: was an anaesthesia faculty who had good understanding of using the ultrasound machine and had previously done at least 10 tracheal ultrasonography during intubation.

2. Airway management/ Intubation: was done by a second or third year anaesthesia resident.

3. Supervising anaesthesia faculty: who supervised the airway management and intubation.

4. Anaesthesia resident or an anaesthesia assistant: injected drugs for induction of anaesthesia and watched the capnogram in monitor.

5. Researcher: noted down the time taken for confirmation by both methods. Also inspected for changes in vitals that would exclude the participant out of the study.

Inside the operating room the ultrasound machine was kept on the left hand side and in line with pelvis of the patient. The ultrasound operator was on the right hand side of the patient and in line with patient's xiphisternum. The blinding was done such that the person reading capnogram would face away from the ultrasound machine, and the ultrasound operator would be facing away from the capnograph monitor.

Patient was placed supine comfortably in the operating table. Continuous ECG and SPO_2 monitoring, 5 minute interval NIBP monitoring or continuous invasive blood pressure monitoring when available was done. A running intravenous drip of crystalloid solution; Ringer's Lactate, Normal saline or Plasmalyte as required was started. Injection Fentanyl 2 microgram per kg was given intravenously. Then Injection Propofol 2 milligram per kg was given intravenously in TUTH and non-cardiac surgery patients in MCVTC, and Injection Etomidate 0.3mg per kg intravenously was given to cardiac surgery patients in MCVTC for induction. Induction of anaesthesia was complete after patient became unresponsive with central mid-dilated pupil and absence of eye lash reflex.

Manual bag and mask ventilation adequacy was then checked. Injection Vecuronium 0.1 milligram per kg was given intravenously, and the stopwatch was started. Manual bag and mask ventilation was continued by the primary intubating resident and assisted by the supervising anaesthesia faculty as needed.

High frequency linear ultrasound probe, 9-13 Megahertz, was placed transversely just above the suprasternal notch. The probe was shifted slightly cranially or caudally as needed to obtain the best visualization of trachea and oesophagus in the same image.
After 5 minutes of injecting Vecuronium, the researcher reset his stopwatch and announced "start" loudly (start point). Laryngoscopy and tracheal intubation was done by the anaesthesia resident. The ultrasound operator held the probe in the appropriate place as previously determined. If the position of the probe obstructed laryngoscopy,

the probe was shifted caudally and tilted slightly cranially. The study was continued only if the latter ultrasound image could also visualize both trachea and oesophagus.

After intubation, the anaesthesia machine which was preset in volume control mode with tidal volume of 6ml/kg, respiratory rate of 26 breaths per minute (as used by Pfeiffer et al[31] in their study), PEEP zero and inspiration:expiration ratio of 1:2; was then attached to the endotracheal tube via the anaesthesia machine circuit with $ETCO_2$ probe connected at the angle piece of the patient end of the circuit.

The ultrasound operator announced loudly as either "ultrasound positive" for tracheal intubation result, or "ultrasound negative" for oesophageal intubation result. The researcher noted down the time in the data entry proforma sheet (end point for ultrasonography).

The next anaesthesia resident (or anaesthesia assistant) meanwhile watched over the capnogram in the monitor. After 6 mechanical ventilations, he announced loudly as "capnograph positive" for tracheal intubation result, or "capnograph negative" for oesophageal intubation result. The researcher noted down the time in data entry proforma sheet (end point for capnography).

The supervising anaesthesia faculty then auscultated the chest in 5 areas in the order: right supramammary – left supramammary - left axillary – right axillary – epigastrium. The ultrasound operator performed bilateral lung ultrasound in second intercostal spaces in the mid-clavicular line and observed for lung sliding. The final endotracheal tube position in trachea was confirmed when there was presence of bilateral air entry on auscultation and lung sliding on ultrasound. In case of only unilateral air entry and unilateral lung sliding, the endotracheal tube was readjusted for endobronchial intubation and reconfirmed again; the subject was not excluded from the study in the event of endobronchial intubation.

If there was absence of breath sounds with absence of lung sliding and bar-code sign[20] in the ultrasound in bilateral chest regions, reconfirmation further was done by the supervising anaesthesia faculty by performing repeat laryngoscopy and visualizing the position of endotracheal tube in relation to the vocal cords. This repeat reconfirmation was done because post-intubation bronchospasm or mucous plugging could also present with similar auscultation and lung ultrasound finding and thus negate the validity of the study. The supervising anaesthesia faculty would then reintubate himself if tube position in the oesophagus was seen during repeat laryngoscopy. The second intubation was not accounted for in this study.

Participants were also excluded if there was:

- Unanticipated difficult bag and mask ventilation
- Unanticipated difficult intubation or CL grade 3 and 4 cases, use of bougie for intubation.
- Fall in Spo2 (< 90%) before endotracheal tube position confirmation
- Bradycardia (heart rate < 40 beats/min) or hypotension (mean arterial pressure < 60 mm of Hg, systolic blood pressure < 80 mm of Hg) during or prior to intubation
- Tachycardia more than 120 bpm or blood pressure more than 180 mm Hg systolic or 110 mm Hg diastolic during or prior to intubation

There were 36 participants enrolled at MCVTC, out of which 5 of the participants had to be excluded out of the study. One had unanticipated difficult intubation, and the other four had hypotension after induction of anaesthesia. There were 67 participants enrolled at TUTH, out of which 3 participants had to be excluded out of the study. Two subjects had hypotension after induction of anaesthesia. The other one had to be excluded because the ultrasound machine went into hung state. Thus there were 31 subjects from MCVTC and 64 subjects from TUTH. Data collection was terminated once the sample size of 95 was met. Different individuals operated ultrasound on the subjects in this study. Flow diagram of the study is shown in figure 8.

Operational Definitions

Ultrasound positive: meant ultrasound detected tracheal intubation. There was fluttering and movement inside the tracheal acoustic shadow as the endotracheal tube was passed, and by the completion of intubation there was only one comet tail appearing acoustic shadow. Color Doppler ray showed color change inside the acoustic shadow on shaking the endotracheal tube.

Ultrasound negative: meant ultrasound detected oesophageal intubation. There was fluttering and increase in echogenicity in the region of oesophagus as the endotracheal tube was passed. By the completion of intubation, there were two comet tail appearing acoustic shadows, “double-tract sign”. Color Doppler ray was seen outside the trachea on shaking the endotracheal tube.

Capnograph positive: meant capnogram showed regular normal shaped waveforms after 6 ventilations. The outcome was tracheal intubation.

Capnograph negative: meant oesophageal intubation. The capnogram had no waveforms or irregular, bizarre or non-uniform shaped waveforms after 6 ventilations.

After confirmation of the endotracheal tube position, true and false positives and negatives were determined for both the methods as depicted in table 1.

Sensitivity, specificity, positive predictive value and negative predictive value, likelihood ratios; for both ultrasonography and capnography were calculated using their corresponding formulas.[37] The results were extrapolated into confidence intervals using Clopper-Pearson confidence interval.[37]

Table 1. Designation of true and false positives and negatives.

Capnography		**Ultrasonography**	
Tracheal outcome	Oesophageal outcome	Tracheal outcome	Oesophageal outcome
True positive (TP): final position in trachea.	***True negative (TN)****:* final position in oesophagus.	***True positive (TP):*** final position in trachea.	***True negative (TN)****:* final position in oesophagus.
False positive (FP)*:* final position in oesophagus.	***False negative (FN)****:* final position in trachea.	***False positive (FP) :*** final position in oesophagus.	***False negative (FN)****:* final position in trachea.

Sensitivity = TP / (TP+FN).

Specificity = TN / (TN+FP).

Positive predictive value (PPV) = TP / (TP+FP).

Negative predictive value (NPV) = TN / (TN+FN).

Confidence intervals, CI (at 95 % level of confidence): for example for sensitivity

CI = (Sensitivity + 1.96SE, sensitivity – 1.96SE). *Where* SE *is standard error*,

SE for sensitivity = square root of [sensitivity (1 – sensitivity)/(TP+FN)][37]

Accuracy = (TP+TN) / (TP+TN+FP+FN).

(TP=True Positive, TN=True Negative, FP=False Positive, FN= False Negative)

Likelihood ratio of a positive test: was given by

$$LR+ = \frac{\text{sensitivity}}{1 - \text{specificity}}$$

The positive likelihood ratio values corresponded to different probabilities as follows[37]:

Table 2. Interpretation of positive likelihood ratio.[37]

Positive likelihood ratio value	*Probability*
0	Excluded disease.
> 10	Large change in likelihood (or in other words high probability of any individual having a positive result on using the diagnostic test).
5 – 10	Moderate change in likelihood.
2 – 5	Small change in likelihood.
1	No change.

Likelihood ratio of negative test: was given by

$$LR- = \frac{1 - \text{sensitivity}}{\text{specificity}}$$

The negative likelihood ratio values also corresponded to different probabilities as follows[37]:

Table 3. Interpretation of negative likelihood ratio.[37]

Negative likelihood ratio value	*Probability*
infinity	Excluded normality.
< 0.1	Large change in likelihood (or in other words high probability of any individual having a negative result on using the diagnostic test).
0.1 – 0.2	Moderate change in likelihood.
0.2 – 0.5	Small change in likelihood.
1	No change.

Data collection and management

The Pre-anaesthetic (PAC) form of the Department of Anaesthesiology, MMC, IOM; (Appendix A) was used to evaluate patients for inclusion into the study. All participants' data such as gender, age, ethnicity, diagnosis, BMI, weight, ASA status, medical comorbidities, airway examination was collected on data entry proforma sheet (Appendix C). The proforma sheet also recorded the baseline vitals and the vitals after induction of anaesthesia and after intubation. The results for ultrasonography and capnography, the respective time taken to obtain the results were recorded in the proforma sheet.

Data entry was done into Microsoft excel 2010. (Appendix E)

Statistical Analysis

Descriptive variables were expressed as mean ± standard deviation, median, range, interquartile range, frequency, percentage and proportion. The calculations were done in Microsoft excel 2010.

The sensitivity, specificity, positive and negative predictive values, accuracy, along with their confidence intervals and likelihood ratios for positive and negative results were calculated by defining the respective mathematical functions into Microsoft excel 2010.

The mean and median times along with the interquartile range and standard deviations, taken for confirmation by capnography and ultrasonography were calculated using SPSS 23.0. Difference in time was calculated as method 1 (ultrasonography) minus method 2 (capnography) and reported as mean with 95% confidence interval; the results were compared using paired student t-test with p values at 95 % level of significance. The analysis was done using SPSS 23.0.

Kappa statistic was used to see agreement over and above that which would have occurred just by chance between these two methods. The kappa (ꝁ) value was calculated using SPSS 23.0. It was interpreted based on the following criteria[38]:

Table 4. Intepretation of kappa value.[38]

Kappa value (ꝁ)	*Degree of agreement*
0.81 - 1.00	Very good.
0.61 - 0.80	Good.
0.41 - 0.60	Moderate.
0.21 - 0.40	Fair.
<0.20	Poor.

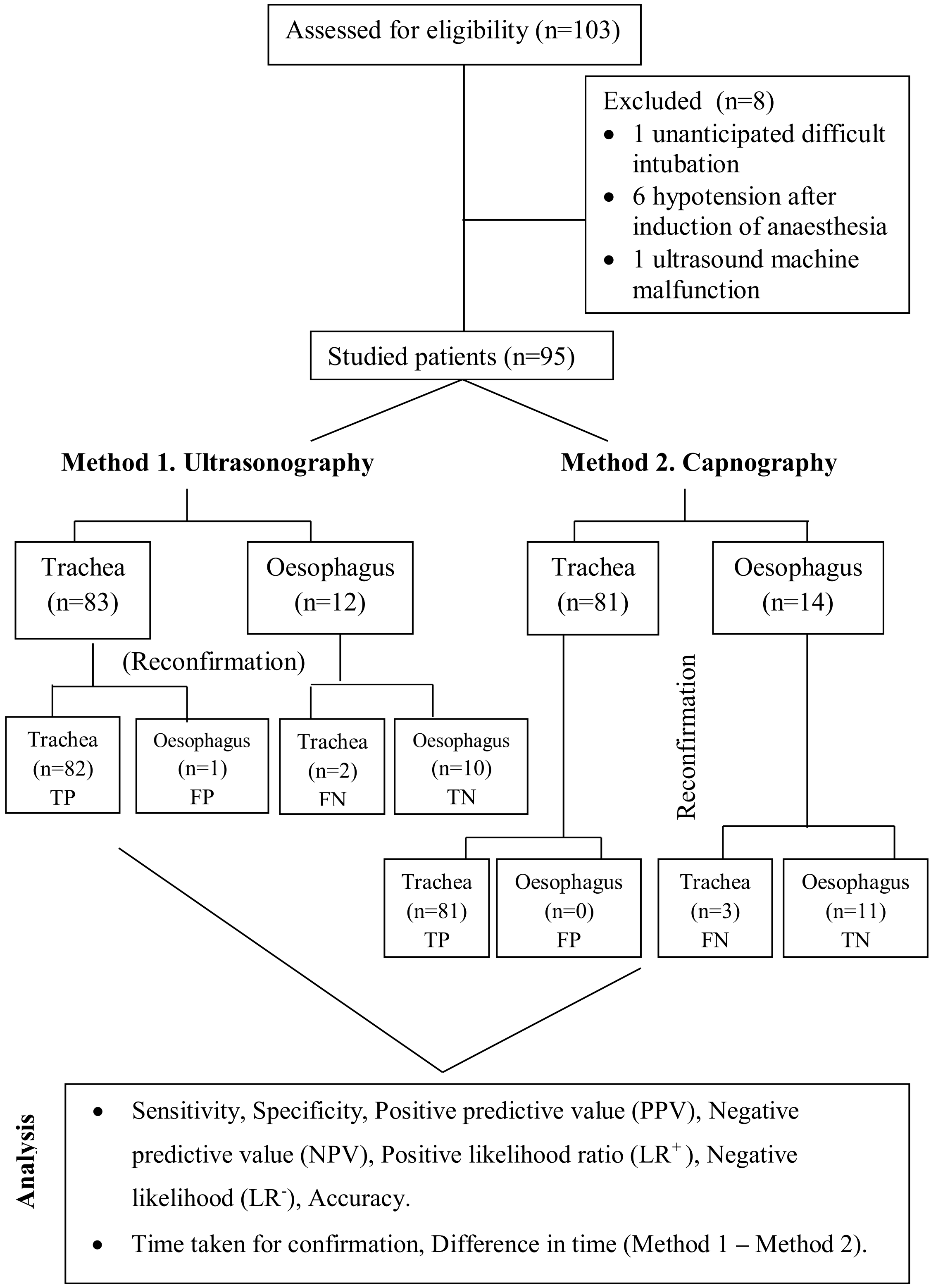


Fig. 8. Study flow diagram.

(TP=True Positive, FP=False Positive, TN=True Negative, FN=False Negative)

RESULTS

Descriptive data

Demography

Among the 95 subjects, the mean age was found out to be 44.24 years with standard deviation of ± 16.18 years, and the median age was 47 years. The youngest patient was of 16 years, and the eldest patient was 85 years old. Most patients were in the age group of 41 to 50 years.

Table 5. Demographic profile according to age.

Mean ± SD (in yrs)	Median (in yrs)	Maximum (in yrs)	Minimum (in yrs)
44.24 ± 16.18	47	85	16

(n=number, SD= Standard Deviation, yrs = years)

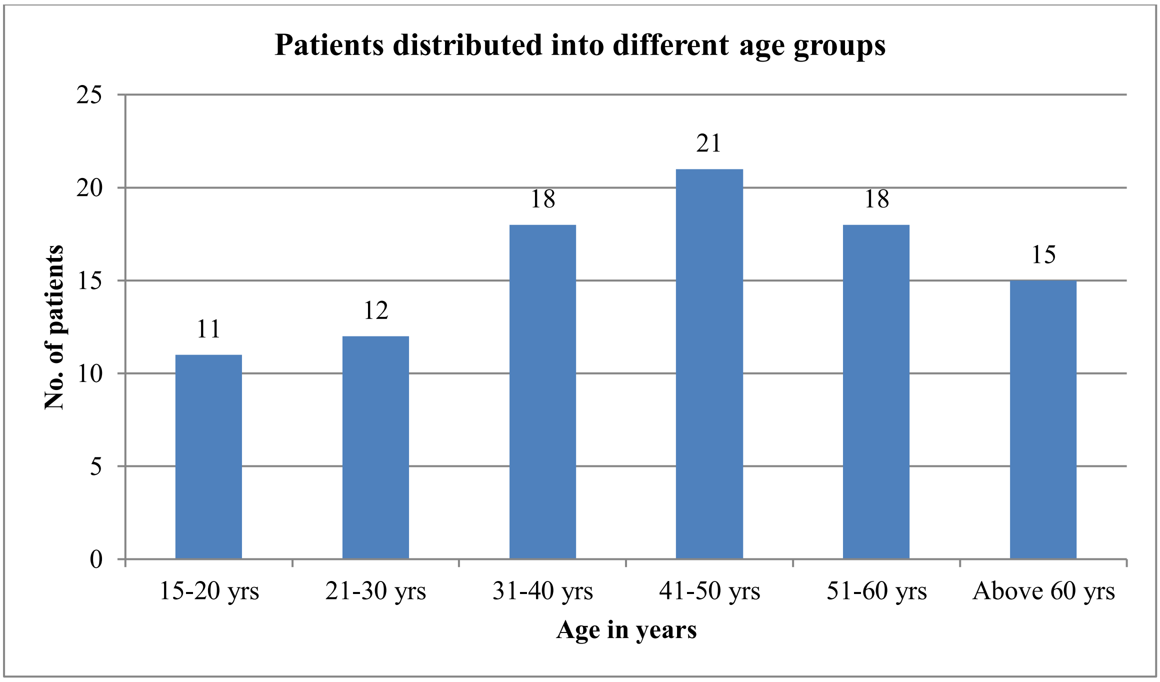


Fig. 9. Distribution of the subjects into different age groups.

Among the 95 subjects, there were 51 females (53.68%) and 44 males (46.32%) in this study.

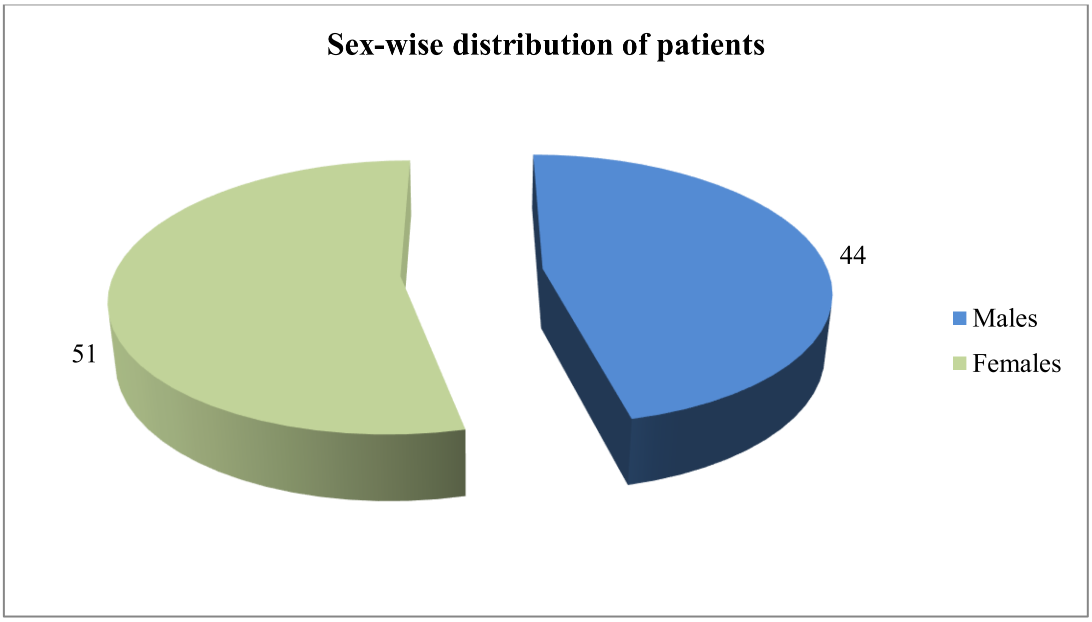


Fig. 10. Sex-wise profile of patients in the study.

The majority of patients were Brahmins (40%), followed by Chhetris (22.10%), Newars (14.70%), Magars (7.36%), and others (15.84%); as shown in figure 11. Others include Rai (4), Bhaisnav (1), Chaudhary (1), Muslim communities (2), Lama (2), Gurung (1), Damai (1), Tamang (2), Thakuri (1) and Sherpa (1).

BMI

The mean body mass index (BMI) of the 95 patients was found to be 23.55 ± 3.58 (mean ± standard deviation); the median BMI was 23.72 and the inter-quartile range [20.68 - 25.92], all values expressed in kg/m^2. The summary is shown in table 3 and figure 12.

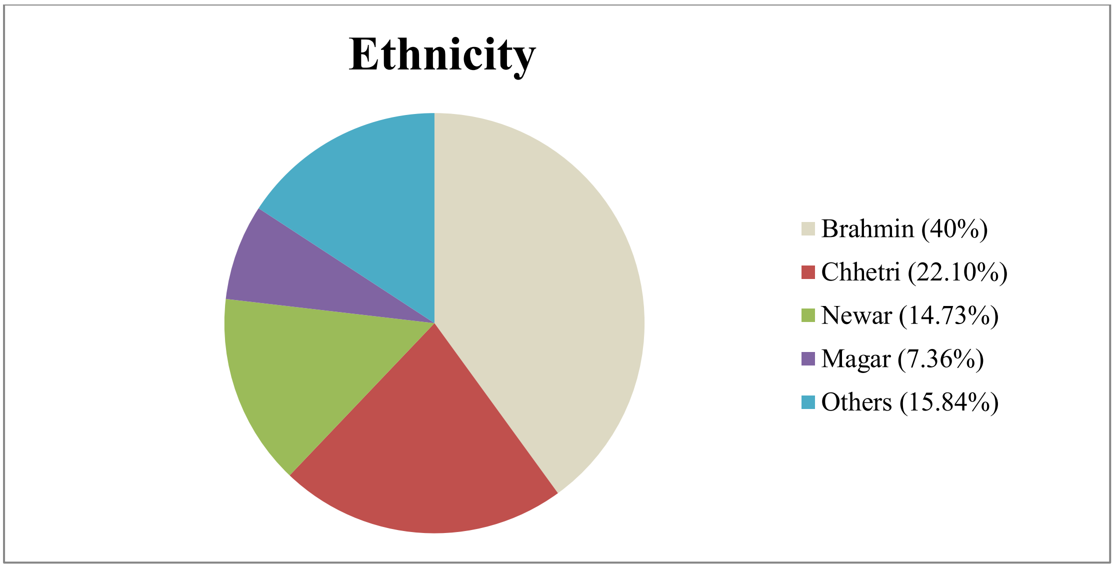


Fig. 11. Distribution of patients as per ethnicity in this study.

Table 6. Average body mass index (BMI) of patients.

	Mean ± SD	Range	Median	IQR
BMI (kg/m^2)	23.55 ± 3.58	16.33 - 33.88	23.72	[20.68 - 25.92]

(SD = Standard Deviation, Range = Maximum - minimum values; IQR = Interquartile range)

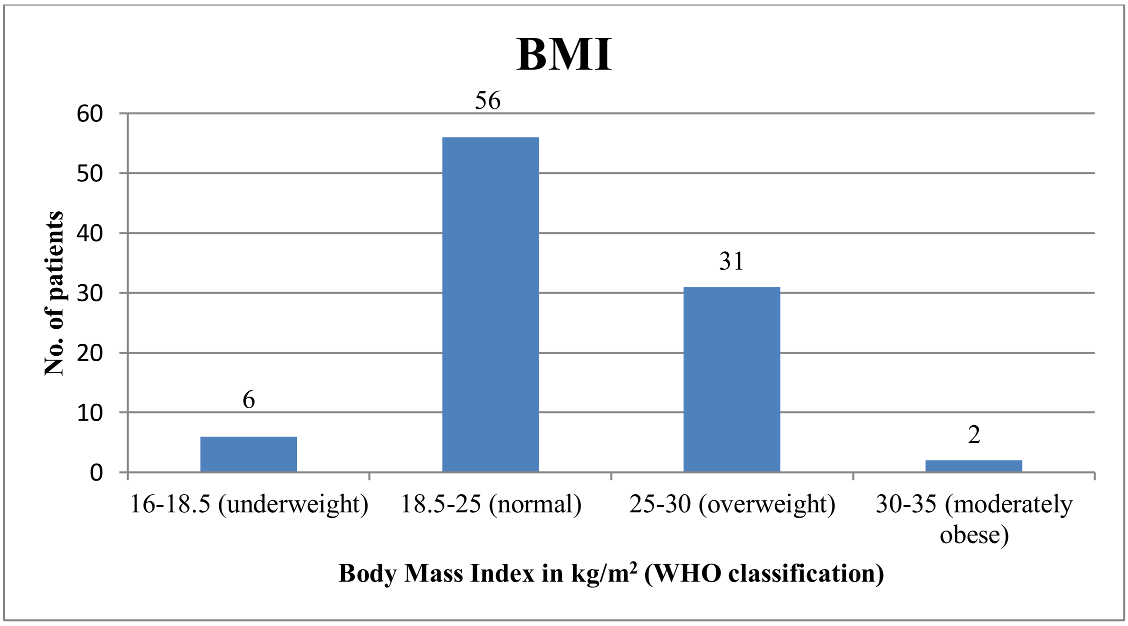


Fig. 12. Frequency of patients according to WHO classification of BMI.

ASA Physical Status

There were 46 ASA I patients and 49 ASA II patients in this study. The clinical conditions in patients with ASA II status are listed below in table 4. Table 4 does not account for the presence of multiple clinical conditions in the patients.

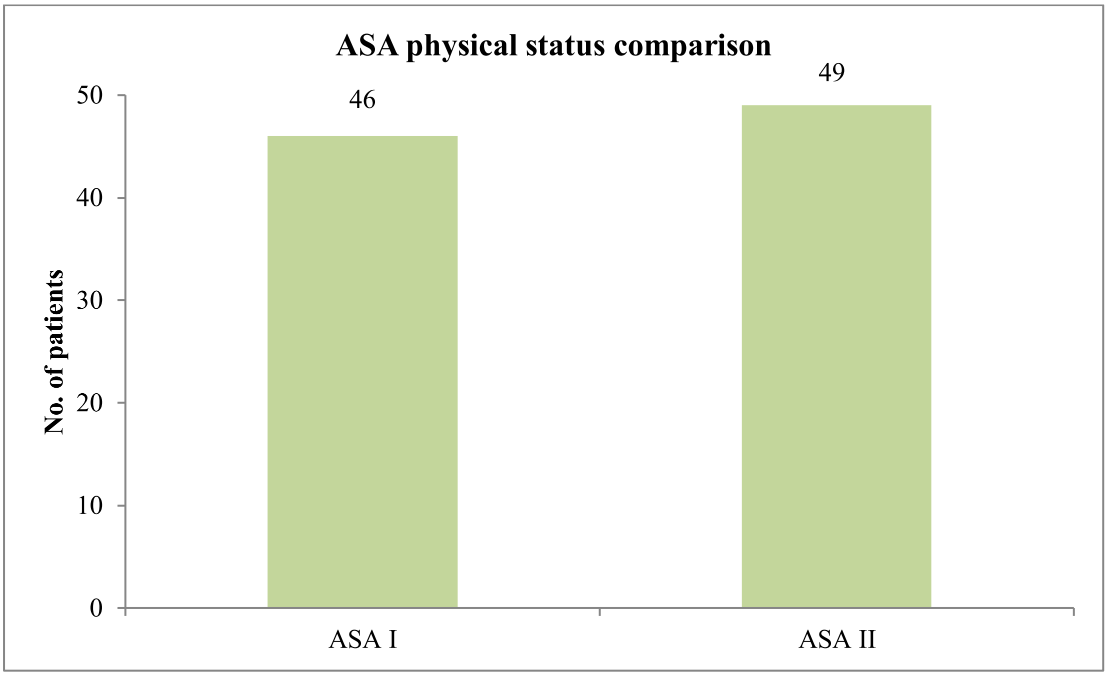


Fig. 13. ASA Physical status distribution of patients.

Table 7. Clinical conditions in ASA II patients.

	No. of patients	
	MCTVC	TUTH
Valvular heart disease	8	0
Coronary heart disease	14	1
Vascular disease	6	0
Hypertension	14	6
Diabetes Mellitus	4	1
Hypothyroidism	3	3
Hepatitis C positive	0	1
Central nervous system disease	0	8

Analytical Statistics and Data

Out of the total 95 intubations, there were 11 oesophageal intubations. The incidence of oesophageal intubation was 11.57% in this study.

Ultrasonography

Ultrasound falsely detected one oesophageal intubation as tracheal, and two tracheal intubations as oesophageal.

Table 8. Distribution of positives and negatives for ultrasonography.

Position showed by Ultrasound	*Endotracheal tube position confirmation*		Total
	Trachea	Oesophagus	
Trachea (n)	TP = 82	FP = 1	83
Oesophagus (n)	FN = 2	TN = 10	12
Total	84	11	n = 95

(n=no. of patients, TP=True Positives, FP=False Positives, FN=False Negatives, TN=True Negatives)

The sensitivity, specificity, positive predictive value and negative predictive value (with their corresponding 95% confidence intervals in round brackets) were calculated to be 97.62% (91.66% - 99.71%), 90.91% (58.72% - 99.77%), 98.80% (92.67% - 99.81%) and 83.33% (55.66% - 95.22%) respectively. The positive likelihood ratio was 10.74, which suggested a large change in the likelihood of positive result. The negative likelihood ratio was 0.03 which also suggested a large change in the likelihood of negative result. The accuracy of ultrasonography in confirming endotracheal tube placement was 96.84% (92.92% - 100%).

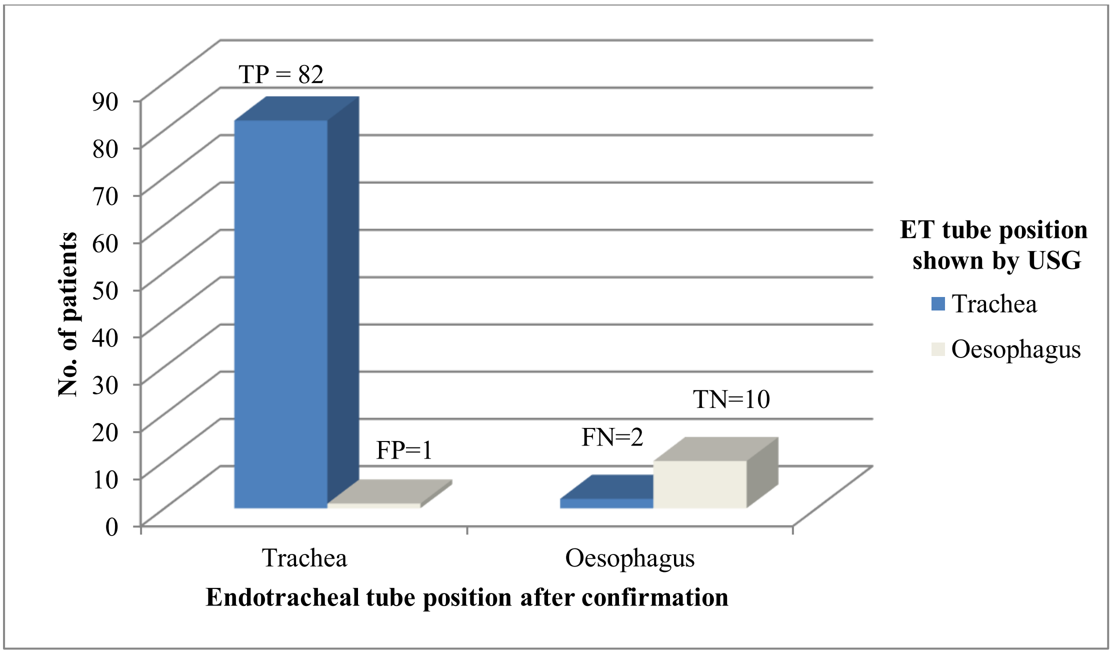


Fig. 14. Distribution of positives and negatives for ultrasonography.

Capnography

There were three false negative results given by waveform capnography. There was no false positive result.

Table 9. Distribution of positives and negatives for capnography.

Position showed by waveform capnography	*Endotracheal tube position confirmation*		Total
	Trachea	Oesophagus	
Trachea (n)	TP = 81	FP = 0	81
Oesophagus (n)	FN = 3	TN = 11	14
Total	84	11	n=95

(n=no. of patients, TP=True Positives, FP=False Positives, FN=False Negatives, TN=True Negatives)

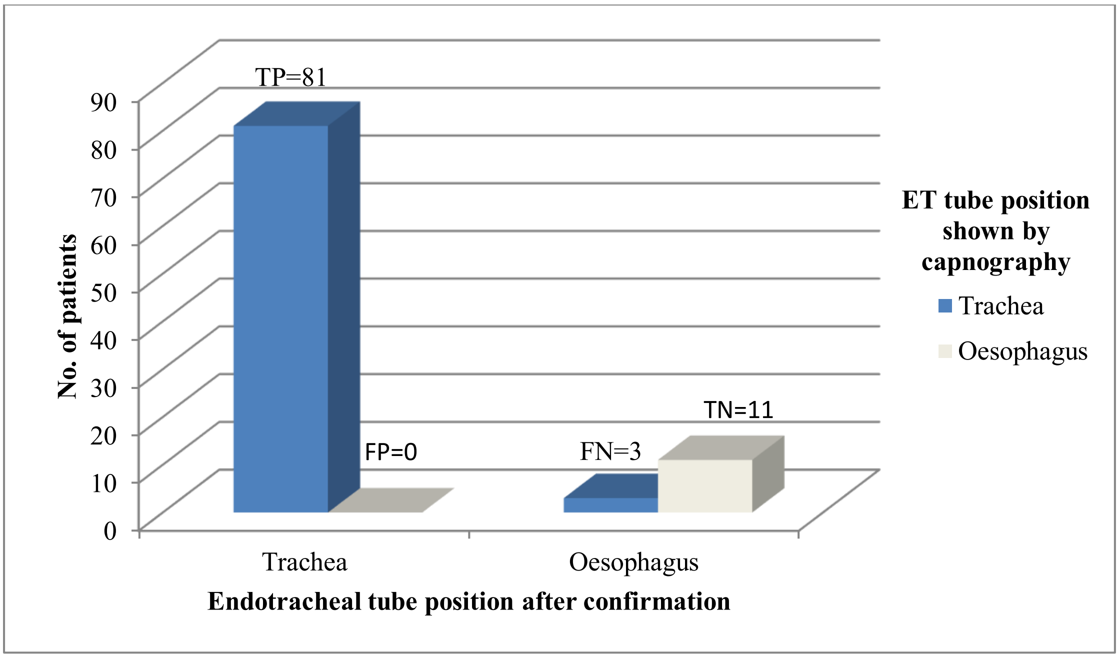


Fig. 15. Distribution of positives and negatives for capnography.

The sensitivity, specificity, positive predictive value and negative predictive value (with their corresponding 95% confidence intervals in round brackets) of capnography were calculated to be 96.43% (89.92% - 99.26%), 100% (71.51% - 100%), 100% (100% - 100%) and 78.57% (54.69% - 91.76%) respectively. The positive likelihood ratio was infinity. The negative likelihood ratio was 0.04 which suggested a large change in the likelihood of negative result. The accuracy of capnography in confirming endotracheal tube placement was 96.84% (92.92% - 100%).

Both ultrasonography and waveform capnography were found to be good, reliable and fairly accurate diagnostic methods of confirming endotracheal tube position. Ultrasonography was comparable diagnostically with capnography for endotracheal tube confirmation. The comparisons of the pretest and posttest probabilities of the two methods are shown in table 10.

Table 10. Comparison of the diagnostic characteristics of ultrasonography and waveform capnography.

	Ultrasonogrpahy	Waveform Capnogrpahy
Sensitivity in % (95% CI)	97.62 (91.66- 99.71)	96.43 (89.92 - 99.26)
Specificity in % (95% CI)	90.91 (58.72 - 99.77)	100 (71.51 - 100)
PPV in % (95% CI)	98.80 (92.67- 99.81)	100 (100 – 100)
NPV in % (95% CI)	83.33 (55.66 - 95.22)	78.57 (54.69 - 91.76)
Accuracy in % (95% CI)	96.84 (92.92 - 100)	96.84 (92.92 - 100)
Positive likelihood ratio	10.74	Infinity
Negative likelihood ratio	0.03	0.04

(CI= Confidence Interval, PPV= Positive Predictive Value, NPV= Negative Predictive Value)

Both ultrasonography and capnography together had correctly identified 10 out of the 11 oesophageal intubations. The 84 tracheal intubations were correctly identified by both ultrasonography and capnography or either one of these methods. Using the same formula (page 35), the combined accuracy of both the methods together was 98.94% (94 divided by 95, in percentage).

The analysis of agreement between the ultrasonography and capnography results was done using Cohen's kappa statistics. A kappa value of 0.749 with 95% confidence interval of (0.567 – 0.931) and standard error of 0.093 was found. The kappa value therefore showed a good agreement between the result of these two methods.

Time taken for endotracheal tube confirmation

Real-time ultrasonography was faster than waveform capnography for endotracheal tube confirmation in all cases. The mean time for confirmation by ultrasonography was 26.79 ± 7.64 seconds (mean ± standard deviation). The mean time for confirmation by capnography was 43.03 ± 8.71 seconds.

The mean difference in time was 16.36 seconds (95% CI: 15.70sec – 17.02 sec). The median difference in time was 16 seconds. The standard deviation in difference in time was 3.23 seconds. The standard error of mean (SEM) was 0.332 seconds. The difference in time was highly significant (p = 0.011).

Table 11. Time taken for endotracheal tube confirmation.

	Range (in seconds)	Mean ± SD (in seconds)	Median (in seconds)	IQR (in seconds)	p-value
Time taken by ultrasonography	14 - 50	26.79 ±7.64	26.00	[15 - 37]	
Time taken by capnography	27 - 67	43.03 ±8.71	42.00	[29 - 55]	
Difference in time (ultrasonography - capnography)	9 - 24	16.36 ±3.23	16.00		0.011

(SD = Standard Deviation, IQR = Inter-Quartile Range, Range = Maximum-minimum values)

A subgroup analysis was done to test whether the time delay in sidestream capnograph could have affected the p-value obtained in difference in time. Two subgroups were divided: one subgroup in which sidestream capnography was used, and the other subgroup in which mainstream capnography was used. There were 37 patients in the mainstream subgroup and 58 patients in the sidestream subgroup. The median time for confirmation of endotracheal tube position in mainstream subgroup was 37 seconds. The median time for confirmation of endotracheal tube position for capnography in sidestream subgroup was 45.5 seconds. The findings of difference in time between ultrasonography and capnography methods in these subgroups are summarized in table 12.

Table 12. Subgroup analysis for difference in time taken for endotracheal tube confirmation.

Difference in time (ultrasonography-capnography)	Range (in seconds)	Mean ± SD (in seconds)	Median (in seconds)	p-value
Mainstream subgroup (n=37)	9 - 19	14 ± 2.62	14	$p < 0.01$
Sidestream subgroup (n=58)	12 - 24	17.87 ± 2.64	17.50	$p < 0.01$

(SD = Standard Deviation, Range = Maximum - minimum values)

The distribution was found to be normal in both subgroups on applying Shapiro-Wilk test ($p < 0.01$). Student's t- test was used to determine the p-value of difference in time to confirm endotracheal tube position between the two subgroups. The p-value, $p< 0.01$ was obtained in both the subgroups, which meant that use of sidestream capnography with a delay time did not affect the significant difference in time between ultrasonography and capnography found in this study.

DISCUSSION

Both ultrasonography and waveform capnography were found to be reliable and accurate methods of confirming endotracheal tube position in this study. The variables that were studied and analyzed in this study are now discussed further.

Descriptive data

The results of this study were not affected by the demographic and physical health profiles of the subjects.

In this study, the patients that were included had ages ranging from 16 to 85 years. Most patients were between 41 to 50 years of age. The median age of the patients was 47 years. There were more females than males in this study, male: female ratio being 44:51 (or 1:1.16).

Elderly patients could have calcifications in thyroid cartilage and trachea, and females could have large thyroid glands which could create artifacts and unclear acoustic shadow in neck ultrasound.[18,20] However external neck examination and chest x-ray assessment of lower neck when available had been done during pre-anaesthetic check-up. Before laryngoscopy was done, the ultrasound probe had examined the lower anterior neck for the best view for the study during which these conditions were ruled out. Thus, the demographic profile did not affect the outcomes of this study.

According to the WHO classification for body mass index (BMI), 31 out of the 95 patients (32.63%) in this study were overweight and 2 patients (2.1%) were morbidly obese. Obesity can lead to thick neck with increased fatty soft tissue mass and edema within the airway, which can create unclear acoustic image. However patients with anticipated difficult airway were not included in this study. Pre-anaesthetic (PAC) examination excluded patients with mouth opening less than three finger breadths of the patient, restricted temporo-mandibular joint movement, stiff cervical neck flexion and extension movements, Mallampati grades II and above, mobile teeth, edentulous upper or lower jaw, upper lip bite test grade III, thyromental distance < 6.5 cms, thyromental height < 3 finger breadths of the patient and neck circumference > 40 cms.

Though there were more ASA II patients than ASA I, the ASA physical status classification did not affect the objectives of this study because any clinical condition that could affect the outcome of the study had already been previously excluded. Clinical conditions that could lead to hypoxemia or change in the exhaled CO_2 levels from the lungs, for example obstructive or restrictive airway diseases, pneumothorax, pleural effusion, malignancy had been excluded.

Hence these descriptive variables did not affect the outcome of the study. These variables reflect the demographic profile of the patients served at the academic centres of IOM in Maharajgunj and provide validity to the study. This data could help as reference for researchers who might carry out similar studies in the same centres in future.

Analytical Statistics

The incidence of oesophageal intubation was 11.57% in this study. Reported incidence of oesophageal intubations during elective intubation is less than 2%.[12,39] The incidence of oesophageal intubation increases up to 6 - 16 % during in-hospital emergency intubations.[29,30,39,40]

Ultrasonography

In this study, the sensitivity, specificity, positive predictive value and negative predictive value (with their corresponding 95% confidence intervals) of ultrasonography were calculated to be 97.62% (91.66% - 99.71%), 90.91% (58.72% - 99.77%), 98.80% (92.67% - 99.81%) and 83.33% (55.66% - 95.22%) respectively.

The sensitivity of ultrasonography in this study is comparable to sensitivity reported in the meta-analyses done by Das et al[21] and Chou et al[6], which were 98% and 93% respectively. The specificity was 90.91% in this study, which is slightly lower compared to the above mentioned meta-analyses where specificity ranges from 97 to 98%.[6,21] But the 95% confidence interval of specificity in this study extends from 58.72 to 99.77% which covers the reported specificity 97 to 98% in these meta-analyses. Thus the calculated pretest probabilities of ultrasonography in this study were not different from those reported in literature.

The PPV and NPV of ultrasonography calculated in this study were 98.8% and 83.33% respectively. The PPV of ultrasonography in this study is similar to that found by Adi et al[30], Chou et al[28], Chintamani et al[34] and Nasreen et al[33]: the reported PPV ranges from 98 to 100% in these studies. The NPV of ultrasonography has been reported to be: 62.5% by Chintamani et al[34], 75% by Adi et al[30], 94% by Chou et al[28], and 96.77% by Nasreen et al[33]. The 95% confidence interval of NPV of ultrasonography in this study was (55.66%- 95.22%), which is comparable to the NPV found by the above mentioned studies.

Ultrasonography had an accuracy of 96.84% in endotracheal tube confirmation in this study. Similar accuracy ranging from 97 to 98% had also been found by previous researchers.[28,30,33]

There are various ways of using ultrasonography for endotracheal tube confirmation.

At the level of vocal cords, the fluttering of vocalis ligament or a change in the position of vocal cords can be observed as the endotracheal tube passes through. But this method was found to be less accurate by Singh et al[41], the accuracy of this technique was 71% in their study.

Dynamic real-time as well as static ultrasound can be done at the level of transcricothyroid membrane and the suprasternal area for endotracheal tube confirmation. Most studies have used static ultrasound after passing the endotracheal tube due to the argument that the ultrasound probe position interferes with the act of laryngoscopy.[28,30] This could be more true for transcricothyroid ultrasonography because of the more cranial location of the probe. But tilting the probe can mitigate the matter provided that the new image shows the desired structures clearly as well. Real-time ultrasound has been found to be very effective and rarely hampering the process of intubation using laryngoscopy. In the meta-analysis done by Chou et al[6], tracheal ultrasonography performed in real-time was associated with superior sensitivity (0.94, 95% CI: 0.86 – 0.98) than that performed in a static (post-intubation) manner (0.91, 95% CI: 0.70 – 0.98). Werner et al[42] did a pilot study and found the sensitivity and specificity of real-time ultrasound at suprasternal level in cadavers to be both 100%. Similar type of study done by Karacebay et al[27] in patients during emergency intubation yielded high sensitivity and specificity of real-time transtracheal suprasternal ultrasound, the results being 97% and 88% respectively. Milling et al[43] found the specificity and sensitivity of real-time transcricothyroid ultrasound to be 100% and 97% respectively. Ma et al[44] did both real-time and static post-intubation ultrasound examination at transcricothyroid level to check endotracheal tube position in human cadavers and they found that diagnostic reliability of real-time ultrasound to be better than that of static evaluation; sensitivity and specificity of real-time ultrasound was 97% and 100% respectively, compared to 51% and 91% for static ultrasound.

Similarly good diagnostic accuracy and reliability have been found with static ultrasound in human subjects during emergency intubations. Adi et al[30] used transcricothyroid ultrasound in longitudinal or transverse probe position as appropriate after emergency intubation and Chou et al[28] used transverse suprasternal static ultrasound after intubation to confirm endotracheal tube position in their studies. Both techniques were found to be accurate and reliable.

Lung ultrasound to see for lung sliding can also be used to confirm endotracheal tube position. Weaver et al[45] found this method to be accurate with results similar to transtracheal ultrasound methods in detecting endotracheal tube position in cadavers. Pfeiffer et al[31] found this method to be accurate and reliable in anaesthesized patients in an operating room.

Real-time suprasternal transtracheal ultrasonography in transverse orientation was used in this study. For reconfirmation of endotracheal tube position we used auscultation along with lung sliding since auscultation alone is not a reliable method of endotracheal tube confirmation.[3,26,46] However, if there was absence of breath sounds with absence of lung sliding in bilateral chest regions, another reconfirmation was done by performing repeat laryngoscopy and visualizing the position of endotracheal tube passing through the vocal cords. This reconfirmation was done because post-intubation bronchospasm or mucous plug could also present with similar auscultation and lung ultrasound finding. Direct visualization is also regarded to be gold standard by few authors.[3,4] On reconfirmation if endotracheal tube position was tracheal, repeat laryngoscopy was not done considering the possibility of airway trauma on repeat manipulation.

There were two false negative and one false positive result with ultrasonography. In case of one of the false negatives, the ultrasound operator had to adjust the probe position because the intubating resident was having difficulty in doing laryngoscopy due to interference by the ultrasound probe. However, the latter ultrasound image had clearly showed both tracheal acoustic shadow and oesophageal oval shaped hyperechocity. Ultrasound probe adjustment had to be done in 5 other cases as well, all of whom in which ultrasound had produced true results anyway. So ultrasound probe adjustment itself was unlikely to have caused false result in this case.

In both false negative cases, the acoustic shadow post intubation was unclear and seemed to have two different artifacts; the color Doppler ray was seen between the two artifacts. Such artifacts might have been caused by calcifications in the thyroid gland or tracheal cartilages and soft tissues.[18] The artifacts might also have been caused by reverberations produced by particulate matter like dirt or sand between the probe and skin. Subcutaneous emphysema can also produce artifacts.[18] However, all these factors had been well accounted for. An uncontaminated ultrasound jelly was used to get a uniform thick layer over the probe to maximize probe to skin contact via the gel medium. The ultrasound probe had scanned the lower anterior area of neck before laryngoscopy to rule out calcifications, masses, emphysema etc.

In case of the false positive result, the acoustic shadow had become unclear after intubation but had not widened. The color Doppler ray appeared inside the acoustic shadow on shaking the endotracheal tube. There had been no need for adjustment of the ultrasound probe position in case of the false positive subject. This false result might have occurred due to the cervical spine movement during laryngoscopy rendering the oesophagus to lie just posterior to the trachea instead of posterolateral relation, thus rendering only a single acoustic shadow.[17]

A large change in likelihood for either a positive or a negative result meant that for any individual, the probability of the endotracheal tube being in the trachea was very high if ultrasound showed tracheal intubation. And the probability of the endotracheal tube being in the oesophagus was very high if ultrasound showed oesophageal intubation.

The average time taken by ultrasonography for assessment of endotracheal tube position in this study was 26.79 ± 7.64 (mean ± SD) seconds.

As different individuals performed ultrasonography in this study, variations in time taken for endotracheal tube confirmation by ultrasonography occurred due to inter-operator differences as well.

The median operating time of static post-intubation ultrasound was found to be 9 seconds with IQR [6 – 14 sec] by Chou et al[28] in their study. This was significantly faster than transcricothyroid static ultrasound for endotracheal tube confirmation done by Adi et al[30]; their median time was 16.40 seconds. The results of these studies cannot be compared with this study because the beginning of laryngoscopy was taken as the start point for time assessment in this study. These studies started their assessment after intubation. The time for laryngoscopy is directly operator dependent and thus the time taken for assessment of endotracheal tube position directly increases with more time spent on doing laryngoscopy and intubation in this study.

Capnography

The sensitivity and specificity of capnography to detect endotracheal tube position was found to be 96.43% and 100% respectively in this study. This was similar to aggregate sensitivity and specificity of 93% and 97% found by Li in his meta-analysis.[24] This meta-analysis included trials which used any form of end tidal CO_2 detection device in adult human subjects. We have used only waveform capnography which is the gold standard; colorimetric and quantitative $ETCO_2$ are less accurate than waveform capnography.[3,7,8,12]

There were three false negative results in capnography. Two of the three false negative results occurred while using sidestream capnography at TUTH and the other false negative result occurred at MCVTC which also had sidestream capnography. There were more than two irregular waveforms during the first six ventilations in these false negative cases.

The false negatives might have occurred in the sidestream capnographs because these are more likely to be blocked due to fogging or misting[2,7] such that the sampling line gas flow could have been obstructed. At MCVTC, after about 15 irregular waveforms, there was no waveform seen for about the next 90 seconds followed by presence of regular waveforms thereafter. This might be due to auto calibration of the capnograph, the occurrence of which during intubation might have produced false negative result.
Other causes like compromised pulmonary blood flow and bronchospasm can also lead to false negative results.[3,9,10] Patients who had hypotension after induction of anaesthesia that could lead to compromised pulmonary flow, were excluded from this study. Bronchospasm would be identified by auscultation or high peak airway

pressure displayed in the ventilator. Bronchospasm had not occurred in any case during this study.

The median time for confirmation of tube position by capnography was 42 seconds. The maximum and minimum times were 67 seconds and 27 seconds respectively.

As discussed earlier, this time was dependent on the intubation time which was person dependent. To standardize the outcomes and time taken, literature was searched for rate of ventilations suggested during capnography measurement. No guideline or recommendation could be found. Most literature and textbooks have mentioned rates of 10 - 12 manual bag ventilations per minute during capnography.

The endotracheal tube in this study was connected after intubation to a preset ventilator with respiratory rate set at 26 ventilations per minute for standardization. This was excerpted from the study done by Pfeiffer et al[31] who had used the same respiratory rate in their study for standardization. Using a fixed mechanical ventilation rate helped to study time for confirmation more precisely and reliably, as the performance of manual bag ventilations would be individual dependent. Individuals might perform manual bag ventilations faster or slower than the usual rates of bag ventilations. Individuals might deliver larger tidal volumes during manual bag ventilations which could be harmful. Using a fixed mechanical ventilation tidal volume also helped to avoid use of higher tidal volumes in this study.

A ventilation rate of 26 ventilations per minute helped to minimize bias in time taken for confirmation of endotracheal tube by capnography compared to ultrasonography. Using slower ventilation rates could have favoured the results towards ultrasonography being faster than capnography. In event of oesophageal intubation, a high ventilation rate could have led to more abdominal distension in the subjects.

However, during this study, subjects with initial oesophageal intubation did not have abdominal distension or high airway pressures when observed in the ventilator such that nasogastric tube decompression of the stomach would be required. This study had excluded patients at risk of aspiration of gastric contents, and also patients with known cardiopulmonary diseases in whom abdominal distension leading to difficulty in ventilation resulting in hypoxemia and hemodynamic compromise could have occurred.

This study used both sidestream and mainstream capnographs. This was because of availability of different types of capnograph at the study sites. The details of sampling line delay are discussed later.

Ultrasonography vs Capnography

Both ultrasonography and waveform capnography were found to be good, reliable and fairly accurate diagnostic methods of confirming endotracheal tube position. Though ultrasonography and capnography were equally sensitive and capnography seemed more specific; the sensitivity, specificity, PPV, NPV of ultrasonography were comparable (statistically not different as seen by their confidence intervals) to waveform capnography.

The combination of ultrasongraphy and capnography increased precision (accuracy) over using either one of them in this study. Since the studies done previously had compared ultrasonography against capnography as the standard and thus calculated the sensitivity, specificity, PPV, NPV of ultrasound; these were not able to show if ultrasound had increased accuracy over using capnography alone.

Both of these methods are now known to be equally reliable. Hence in case of unmatched result given by these two methods in a patient, a third highly reliable method of confirmation has to be used because both ultrasonography and capnography have statistically not different false positive (1 – specificity) and false negative (1 – sensitivity) rates.

There was generally good agreement between the results produced by ultrasonography and capnography as shown by the kappa value of 0.749 with 95% confidence interval of (0.567 – 0.931). Other studies have shown a good or a very good agreement of these two methods by kappa statistics. The kappa value calculated by Adi et al[30], Chou et al[28], Karacebay et al[27] and Chintamani et al[34] were 0.85, 0.93 (0.84 – 1.00), 0.85 and 0.76 respectively.

Real-time, transtracheal, transverse suprasternal ultrasonography was significantly faster ($p = 0.011$) than capnography by 16.36 ± 3.23 seconds (mean ± SD) in confirming endotracheal tube position in this study. The subgroup analysis between mainstream and sidestream capnographs also showed that the type of waveform capnograph device used did not affect the significant difference in time of ultrasound over capnograph in confirming endotracheal tube position.

The sidestream capnograph at MCVTC had system response time of < 4 seconds, and that at TUTH had system response time of < 3 seconds. Adjusting for rise time of 200 milliseconds (the actual rise time of sidestream capnograph device used at TUTH; the rise time of that used at MCVTC was unknown), the transit time (delay time) would be in between 3 to 4 seconds in MCVTC sidestream capnograph and in between 2 to 3 seconds in TUTH sidestream capnograph. No delay was expected in mainstream capnograph device.

The median time taken for endotracheal tube confirmation by mainsteam capnograph was 37 seconds and that by sidestream capnograph was 45.5 seconds. The combined median time taken for endotracheal tube confirmation by capnography was 42 seconds. The difference in time with ultrasonography was maximum of 19 seconds and minimum of 9 seconds while using mainstream capnograph, and maximum of 24 seconds and minimum of 12 seconds while using sidestream capnograph. These findings correlate to the delay time of sidestream capnographs as mentioned previously. Though theoretically the delay time should not have exceeded 4 seconds, the difference in median time for confirmation between these types of capnographs was 8.5 seconds. The median time for confirmation of endotracheal tube position in this study would be affected by the time taken by the anaesthesia resident for intubation. Thus difference in time for confirmation between the two types of capnographs could be greater or lesser than 8.5 seconds depending on the variability of time taken for intubation in this study.

Few studies have compared if ultrasound can be faster than capnography. Karacebay et al[27] found that dynamic transtracheal ultrasound at suprasternal level combined with lung sliding done by two separate operators simultaneously during intubation, was faster in average by 5.9 seconds than capnography for endotracheal tube confirmation. Pfeiffer et al[31] found that lung ultrasound was in average 7.1 seconds faster than capnography in confirming endotracheal tube position.

The difference in time was greater in this study, likely due to use of sidestream capnograph. But as discussed earlier, this did not affect the significance in difference in time.

Chintamani et al[34] in their study comparing ultrasound and capnography found mean ± SD time for confirmation by ultrasound to be 12 ± 1.31 secs, and that by capnography to be 8.98 ± 1.04 secs. Their finding of capnography being significantly faster is debatable because they used transtracheal ultrasound at suprasternal level first in transverse view then in longitudinal view, followed also by scanning towards the left side of neck to align the area of oesophagus towards the center of probe. They also have not mentioned the criterion for capnography, whether $ETCO_2$ values were used or not, and the number of waves they counted for a result.

LIMITATIONS

1. This study used both sidestream and mainstream capnographs as per availability at the study sites. Sidestream capnographs have a delay time in reading exhaled CO_2, which does not occur in mainstream capnographs.
2. Different persons (anaesthesia faculties with training in airway ultrasound) performed ultrasound imaging in this study.
3. This study did not see if novice ultrasound operators could also confirm endotracheal tube position by ultrasound imaging earlier than capnography.

CONCLUSION

Ultrasonography and waveform capnography are equally reliable and accurate methods of confirming endotracheal tube position. Confirmation of endotracheal tube position by real-time ultrasonography is faster than capnography independent of the ultrasound operator. The combination of ultrasonography with capnography in practice will help reduce time and increase precision of confirming endotracheal tube position.

RECOMMENDATIONS

- Real-time transtracheal ultrasonography is safe and can be used as an alternate method of confirming endotracheal tube position in operating theatres.
- Using real-time transtracheal ultrasound can help confirm endotracheal tube position earlier than capnography.
- Using real-time transtracheal ultrasound will help avoid manual bag ventilations to confirm endotracheal tube position and can prevent aspiration of gastric contents into lungs in cases of oesophageal intubation.

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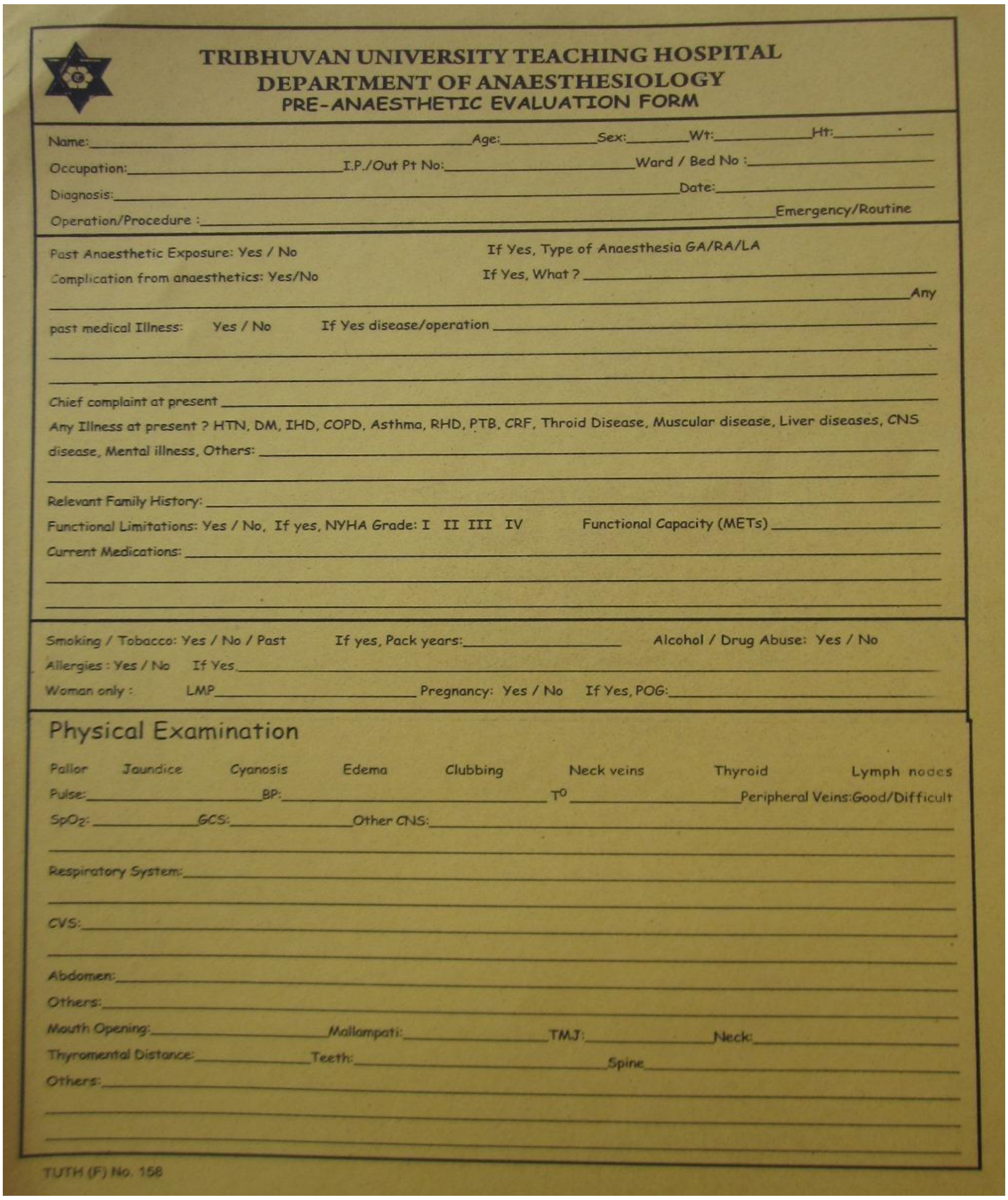
APPENDIX A

Pre-anaesthetic evaluation (PAC) form, Department of Anaesthesiology

Front page:



TRIBHUVAN UNIVERSITY TEACHING HOSPITAL
DEPARTMENT OF ANAESTHESIOLOGY
PRE-ANAESTHETIC EVALUATION FORM

Name:______ Age:______ Sex:______ Wt:______ Ht:______
Occupation:______ I.P./Out Pt No:______ Ward / Bed No :______
Diagnosis:______ Date:______
Operation/Procedure :______ Emergency/Routine

Past Anaesthetic Exposure: Yes / No   If Yes, Type of Anaesthesia GA/RA/LA
Complication from anaesthetics: Yes/No   If Yes, What ?______
______ Any
past medical Illness: Yes / No   If Yes disease/operation ______
______
______
Chief complaint at present ______
Any Illness at present ? HTN, DM, IHD, COPD, Asthma, RHD, PTB, CRF, Throid Disease, Muscular disease, Liver diseases, CNS disease, Mental illness, Others: ______
______
Relevant Family History: ______
Functional Limitations: Yes / No, If yes, NYHA Grade: I II III IV   Functional Capacity (METs) ______
Current Medications: ______
______
______

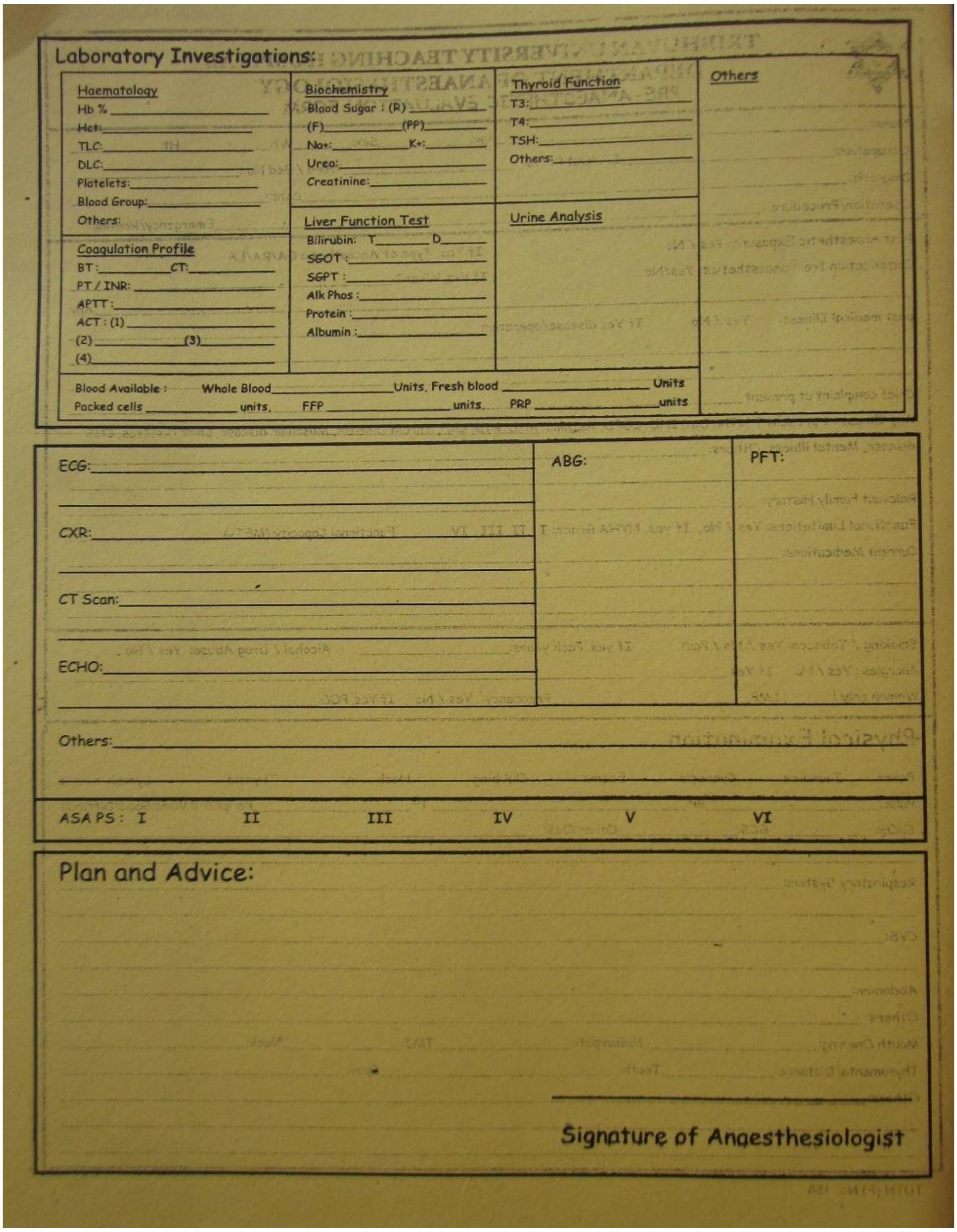
Smoking / Tobacco: Yes / No / Past   If yes, Pack years:______   Alcohol / Drug Abuse: Yes / No
Allergies : Yes / No   If Yes______
Woman only :   LMP______ Pregnancy: Yes / No   If Yes, POG:______

Physical Examination

Pallor   Jaundice   Cyanosis   Edema   Clubbing   Neck veins   Thyroid   Lymph nodes
Pulse:______ BP:______ T⁰______ Peripheral Veins:Good/Difficult
SpO2:______ GCS:______ Other CNS:______
______
Respiratory System:______
______
CVS:______
______
Abdomen:______
Others:______
Mouth Opening:______ Mallampati:______ TMJ:______ Neck:______
Thyromental Distance:______ Teeth:______ Spine______
Others:______
______
______

TUTH (F) No. 158

Back page:



Laboratory Investigations:

Haematology
Hb %
Hct:
TLC:
DLC:
Platelets:
Blood Group:
Others:

Biochemistry
Blood Sugar : (R)
(F) (PP)
Na+: K+:
Urea:
Creatinine:

Thyroid Function
T3:
T4:
TSH:
Others:

Others

Coagulation Profile
BT : CT:
PT / INR:
APTT :
ACT : (1)
(2) (3)
(4)

Liver Function Test
Bilirubin: T D
SGOT :
SGPT :
Alk Phos :
Protein :
Albumin :

Urine Analysis

Blood Available : Whole Blood Units, Fresh blood Units
Packed cells units, FFP units, PRP units

ECG:

CXR:

CT Scan:

ECHO:

ABG:

PFT:

Others:

ASA PS : I II III IV V VI

Plan and Advice:

Signature of Anaesthesiologist

APPENDIX B

CONSENT

Department of Anaesthesiology,

Tribhuvan University, Institute of Medicine, Kathmandu, Nepal.

Study Title: "Ultrasonography imaging versus waveform capnography in detecting endotracheal tube placement during intubation in a tertiary hospital."

Study Number/ Subject's Initials: _______________
Subject's Name:_______________
Date of Birth / Age: _________________

Please do initial in box (Subject)

(i) I confirm that I have read and understood the information sheet and consent form dated __________ for the above study and have had the opportunity to ask questions.

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

(iii) I understand that the researchers and the IRB and other regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published.

I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s)

(v) I understand that there is no financial incentive for the investigator or the institute and hospital. I also understand that in event of any adverse outcome in the process of my stay in the hospital, there will not be any compensation in any form due to my involvement in this study.

I agree to take part in the above study.

Signature (or Thumb impression) of the Subject Right Left

____

Date: _____/_____/______ Signatory's Name: _____/_____/______

Signature of the Investigator: __________________________ Date: _____/_____/______

Study Investigator's Name: ____________________________________

Signature of the Witness _______________________ Date:_____/_____/_______

Name of the Witness: ________________________________

APPENDIX C

Proforma

“Ultrasonography imaging versus waveform capnography in detecting endotracheal tube placement during intubation in a tertiary hospital”.

Conducted by : Dr. Shirish Shakti Maskay, MD Resident in Anaesthesiology, IOM.

Mobile no.: 9841564879.

Preceptor: Prof. Dr. Bishwas Pradhan

Co-guides: Dr. Priska Bastola, Dr. Ninadini Shrestha

Participant serial no. : Date:

Inpatient no.: Centre:

Name/Ethnicity: Age/sex:

Address: Phone:

Weight / BMI : Ward:

Diagnosis:

Planned surgery:

ASA status: Co-morbid conditions:

Ongoing treatment/drugs:

Airway assessment:

Mouth opening/upper lip bite test / mallampati grade/ teeth/ neck circumference

Temporo-mandibular joint/ neck / thyromental distance/ thyromental height

Date of surgery :

Hours of fasting:

Premedication :

IV cannulation: IV fluid:

Induction of general anaesthesia:

Muscle relaxant:

Endotracheal tube type and size: CL grade:

	ECG rhythm	Pulse rate	Blood Pressure	SPO_2
Preop at OT recovery				
Prior to induction				
After induction of general anesthesia				
After intubation				

Endotracheal tube position showed by Ultrasound: Trachea / Oesophagus:

Time taken for tube position result by ultrasound:

Endotracheal tube position showed by Capnography: trachea (6 positive waves) /

oesophagus (absence of positive waves or irregular waves after 6 ventilations)

Time taken for capnography result:

Reconfirmation of tube position: Trachea / Oesophagus

Auscultation

Lung sliding sign

End results for both methods:

Ultrasound: True positive / False positive / true negative / false negative

Capnography : True positive / False positive / true negative / false negative

APPENDIX D

Thesis approval letter from IRB

त्रिभुवन विश्वविद्यालय
चिकित्सा शास्त्र अध्ययन संस्थान
डीनको कार्यालय, महाराजगंज
पो.ब.नं.: १५२४, काठमाडौं, नेपाल ।
फोन नं.: ४४१०९११, ४४१२०४०, ४४१३७२९, ४४१८१८७

Tribhuvan University
Institute of Medicine
Office of the Dean
Maharajgunj, P. O. Box: 1524
Kathmandu, Nepal
Ph.# 4410911, 4412040, 4413729, 4418187

पत्र संख्या / Ref. No.:- 250(6-11-E)2/073/074

Research Department

मिति / Date:- 16 Jan., 2017

Dr. Shirish Shakti Maskey
MD Resident
Department of Anesthesiology
Maharajgunj Medical Campus
Maharajgunj.

Ref: Approval of Research Proposal: Ultrasonography imaging vs waveform capnography in detecting endotracheal tube placement during intubation in a tertiary hospital.

Dear, Dr. Maskey,
Thank you for the submission of your thesis proposal entitled **"Ultrasonography imaging vs waveform capnography in detecting endotracheal tube placement during intubation in a tertiary hospital"** in the meeting of Institutional Review Board, Institute of Medicine, Tribhuvan University on 28 December, 2016.

I am pleased to inform you that the above mentioned research proposal has been approved by Institutional Review Board, Institute of Medicine on 16 Jan., 2017.

As per IRB rules and regulations the investigator has to strictly follow the protocol stipulated in the proposal. Any change in objective, problem statement, research questions or hypothesis, methodology, implementation procedure, data management and budget may be made so and implemented after prior approval from this Research Department and IRB. Thus, it is compulsory to submit the detail of such changes intended or desired with justifications prior to actual change in the protocol.

You are also requested to follow the ethical guideline of IRB, Institute of Medicine.
After completion of your study you must submit a copy of thesis to Research Department.
If you have any further queries, please do not hesitate to contact us.

....
Prof. Dr. Y P Singh
Member Secretary
Institutional Review Board

Research Department
Institute of Medicine
1972

Cc.
HOD
Department of Anesthesiology
Maharajgunj Medical Campus
Maharajgunj.